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Endocrinology

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Internal Secretions

July, 1922

STUDIES ON THE PARATHYROIDS III.

TWO CASES OF COMBINED ENLARGEMENT OF THE THYMUS GLAND AND OF THE LOWER PARATHYROIDS

HILDING BERGSTRAND

STOCKHOLM, SWEDEN

CASE I. SVEA INGEBORG ANDERSSON, 22 YEARS OLD.

The patient was taken into Sabbatsberg Hospital on Nov. 17, 1916, and discharged Jan. 20, 1917. The diagnosis was *appendicitis acuta gangraenosa perforata cum peritonitide purulenta bilat.* During this stay in the hospital she stated that since her 17th year she had suffered from epilepsy. But no closer examination was made except concerning the appendicitis.

The patient was again admitted to the hospital Dec. 14, 1917, and discharged Dec. 19 with the diagnosis, neurasthenia. She stated that from her 17th year she had had attacks when she lost consciousness, fell down, and bit her tongue. The attacks seem generally to have come once a week, but more often if she worked hard. She had had struma for two years and for the same length of time had been troubled with difficulty in breathing as soon as she caught cold. In addition, she seems, during the two months before she entered the hospital, to have had a cough and shortness of breath when going up stairs. During this period the epileptic fits were also frequent. She knew of no hereditary tendency to nervous disorders. The clinical investigation gave very few objective findings. There were found a number of ronchi in the right lung, redness in the throat, and a

struma of average size. The patient was menstruating at the time. All the reflexes were normal. There was no rise in temperature, but a somewhat increased frequency of the pulse, varying between 80 and 100.

The patient was admitted a third time on March 3, 1918, and died a few hours later. When admitted she showed no obvious enlargement of the heart, but a rapid pulse and ronchi above both lungs. When taken into the ward the patient, who did not seem especially ill, suddenly turned blue and died immediately.

AUTOPSY REPORT No. 87: 1918.

On account of the relatives' opposition no autopsy could be made before three days after death. In spite of this the decomposition was slight.

The body weight was 72 kg. and length, 166 cm. The structure of the body was very strong. The shoulders and pelvis were broad. The flesh was well developed but there was no real adiposity. The general color of the skin was pale. The skin showed no changes. The mammae were large. The teeth were normal.

The sawed-off part of the skull weighed 430 grams; it was not quite symmetrical. The tubera frontalia and parietalia were rather thick while other parts of the cranium were thinner. The juga cerebralia was not especially developed. All the bones of the body were hard and firm without any signs of softening.

The dura was of normal thickness. The soft membranes were thin, transparent and smooth. The arteries were thin-walled. The brain weighed 1365 gr. A moderate amount of clear fluid was found in the ventricles. The brain parenchyma was firm. It was evidently slightly hyperemic. The pineal gland weighed 100 mg. and the hypophysis 800 mg.

The heart weighed 280 gr. The myocardium was firm, contracted and brownish-red. The endocardium was smooth and shining, the valves thin and membranous. No changes were seen in the aorta. The mucous membrane in the throat and at the base of the tongue was swollen. The tonsils were enlarged; their mucous membrane, like the surrounding mucosa, was dark red. The laryngeal mucous membrane was not swollen. In the bronchi was a large amount of thick mucous, greyish-yellow fluid. The pleural sacs were empty; the lungs, free; the pleurae smooth and transparent. The right lung weighed 525 and the left, 470 gm. Both were fairly voluminous and rich in fluid, not contracted as usual but stretched out as if they were fixed in the position of inspiration. The pressed-out juice was fairly rich in blood in the back parts but clear everywhere. The parenchyma was pale in the front parts and dark red in the back parts. The lymphatic glands in the hilus of the lung were as large as a brown bean and pale in color. No spots of any kind were found in them and no signs of obstruction in the air-passages.

The liver weighed 1480 gm. and was dark red. Its consistency was normal, as was the surface of the section. The gall-bladder contained dark-green bile. The pancreas was pale and weighed 70 gm.

The mucous membrane of the stomach and intestines was cadaverously stained by blood-pigment; otherwise it was normal.

The peritoneum was smooth and shining all over. There was no appendix. The right kidney weighed 140, the left, 125 gm. The surface beneath the easily loosened renal capsule was smooth. The cut surface was dark red and with fairly distinct markings; its consistency was firm. The uterus weighed 80 gm.; its musculature was somewhat diffusely hypertrophic. The right ovary weighed 10, the left, 6 gm. The latter was attached to the uterus by connective tissue adhesions, which were, however, easily loosened. There was a large corpus rubrum in the right ovary. The cervix was virginal; the vagina was normal.

The spleen weighed 250 gm. Its capsule was somewhat tense, its cut surface dark brownish-red with especially prominent greyish-white follicles. The consistency of the parenchyma was fairly loose. The bone marrow in the diaphysis of the right femur was yellow.

The right adrenal weighed 4.50, the left, 5.75 gm. They showed the ordinary color and structure. The thyroid weighed 28.5 gm. and showed a dark red, firm parenchyma. The thymus weighed 39 gm. Its parenchyma was greyish-white and was very like the parenchyma in an infant. The parathyroids weighed: right upper, 25 mgm., right lower, 310 mgm., left upper, 45 mgm., and left lower, 320 mgm.; the lower were firm, the upper, flaccid.

Fig. 1. Thymus and parathyroids in Case I. Reduced one-half.

Microscopic examination. The spleen showed swelling of the sinus endothelia and the pulp cells. There were no "centres of growth" in the follicles. There was considerable hyperemia.

Pieces of the back parts of the lungs showed in sections patches of coagulated fluid in the alveoli. There was no cellular exudation. The capillaries in these regions were considerably dilated.

The kidneys showed, in relation to the patient's age, an apparently increased number of sclerotic glomeruli in the most superficial layers of the cortex. Around these glomeruli was an infiltration of lymphocytes. Otherwise the vessels, glomeruli, canals and interstices were normal.

The pancreas was very much altered on account of decomposition, especially the islets of Langerhans. The adrenals contrasted sharply with this, as both their medulla and cortex were completely preserved and showed the clear and apparently normal demarcation.

The thyroid showed follicles filled with hard, firm coloid which cracked when sectioned. The epithelium was cubical; there was no extension of the epithelium into the lumen and no adenomatous vegetations or cell infiltrations in the interstices.

The ovaries showed Graafian follicles in different stages of development and corpora lutea in varying stages of regression. The interstitial tissue showed no changes.

The hypophysis and epiphysis were saved for a possible later investigation.

Parathyroids. The two upper parathyroids presented an appearance normal for this age. The parenchyma was compact, i. e., no ingrowing of adipose cells between the follicles had yet taken place. The cells consisted of "principal cells" in different stages of secretion and exceedingly few Welsh's cells. The "principal cells" all showed, with osmic fixation, or when stained with Sudan III, the typically great content of fat. The two lower parathyroids were on the whole identical but differed sharply from the two upper. Frozen sections fixed in osmium immediately showed that the enlargement was caused by a new formation occupying the main body of the glands. This new formation had thrust aside the old tissue, which lay like a thin peel outside the new. The sharp demarcation between the new and the old tissue was due to the fact that the cells of the former were free, or practically free, from fat, while the old cells retained their normal abundance of fat (Fig. 2). On the other hand, there was no capsule around the new formation. In these respects the conditions agreed with what is usually observed in new formations in the parathyroids.

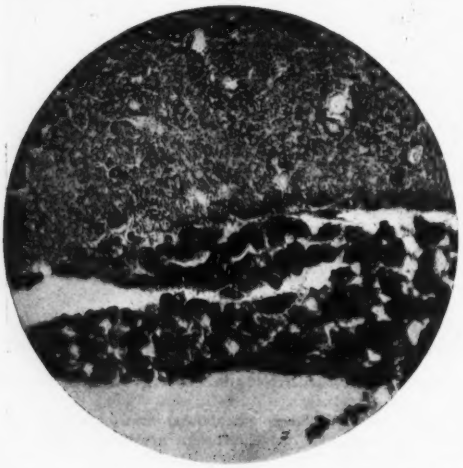


Fig. 2. Lower right parathyroid in Case I. The darker part indicates the old parenchyma, the lighter part, the new growth. The difference is caused by the stained fat in the older parenchyma cells and the presence of large interstitial fat cells in the older tissues. Frozen section. Sudan III-Haematoxylin stain.

I may refer here to photographs in a previous article (1). No typical Welsh's cells were observed in the new formation. On the other hand, there were a number of cells that seemed to be intermediate between "principal cells" and Welsh's cells. (The reason why I consistently use the expression Welsh's cells and not eosinophile cells is that I consider the latter expression misleading. In my opinion (2) the Welsh's cells are degenerated "principal cells" appearing

Table I

	Entire Gland	The Parenchyma	The Cortex	The Medulla	Index	Interstitial Tissue	Hassall's Corpuscles per Mg. of the Parenchyma — Group I	II	III	IV	V	VI	VII	VIII	Total	Hassall's Corpuscles per Mg. of the Medulla — Group I	II	III	IV	V	VI	VII	VIII	Total
21–25 years.	20.60	10.66	6.09	4.57	1.3	9.68	11.3	26.5	13.7	3.9	1.2	0.6	0.04	0.06	57.4	26.3	61.8	31.9	9.0	2.9	1.5	0.09	0.1	133.7
Average minimum and maximum figures (Hammar).	9.50	4.02	2.08	1.94	1.0	5.14	4.2	14.9	10.4	2.2	0.08	0.08	0.	0.	41.8	8.6	30.8	23.2	5.5	0.2	0.2	0.	0.	86.3
	26.48	13.64	8.16	5.85	1.7	13.96	23.2	31.4	24.2	7.8	2.1	1.3	0.1	0.3	75.2	54.2	73.5	50.1	16.3	4.5	2.7	0.3	0.6	175.8
Case I. Age 22 years. Female.	37.4	22.44	11.93	10.51	1.1	14.96	3.3	5.5	2.6	2.1	1.2	0.7	0.	0.	15.4	7.1	11.8	5.5	4.5	2.5	1.5	0.	0.	32.9
56–65 years.	15.02	0.93	0.63	0.53	1.2	14.9	19.0	29.2	21.6	1.8	0.2	0.	0.	0.	71.8	42.7	68.0	49.3	3.8	0.5	0.	0.	0.	164.4
Average minimum and maximum figures (Hammar).	5.6	0.28	0.41	0.13	0.9	5.36	0.	0.	5.5	0.5	0.	0.	0.	0.	19.6	0.	57.0	16.5	1.0	0.	0.	0.	0.	80.1
	24.0	1.87	0.95	0.92	4.3	23.16	42.4	46.3	43.3	3.6	0.8	0.	0.	0.	109.6	82.1	89.6	88.5	8.6	1.0	0.	0.	0.	212.2
Case II. Age 58 years. Female.	27.7	11.60	6.28	5.32	1.2	16.09	0.38	23.3	5.25	9.75	1.48	0.203	0.	0.	40.36	0.84	50.9	11.4	21.3	3.2	0.44	0.	0.	88.08

	The Absolute Number of the Hassall's Corpuscles — Group I	II	III	IV	V	VI	VII	VIII	Sum	The Relation Between Group I and II	Incrusted Hassall's Corpuscles, Corpuscles, Total Number — Pro. Mg. of the Parenchyma	Pro. Mg. of the Medulla	The Absolute Number
21–25 years.	120,310	282,484	145,903	41,340	13,347	6,961	448	624	611,418	1: 2.3	1.3	3.0	13,691
Average minimum and maximum figures (Hammar).	18,492	110,952	97,284	25,542	929	929	0	0	264,516	1: 1.3	0.	0.	0
	254,272	379,192	182,277	71,036	25,284	15,652	1,168	3,504	823,973	1: 6.0	8.6	17.8	36,120
Case I. Age 22 years. Female.	74,052	123,420	58,344	47,124	26,928	15,708	0	0	345,576	1: 1.6	0.	0.	0
56–65 years.	17,745	27,289	20,190	1,669	204	0	0	0	67,097	1: 1.5	3.2	7.1	3,051
Average minimum and maximum figures (Hammar).	0	0	1,320	192	0	0	0	0	4,704	1: 1.0	0.	0.	0
	58,936	64,357	80,971	3,564	420	0	0	0	161,381	1: 2.1	6.9	14.1	12,903
Case II. 56 years. Female.	4,408	270,180	60,900	113,100	17,168	2,354	0	0	468,110	1:61.3	0.	0.	0

normally as a phenomenon of age, while in the parathyroids there are also other "eosinophile" cells forming principal cells filled with secretion and in full activity. Even the old tissue had in this case no Welsh's cells, nor did colloid occur anywhere.

Thymus. This gland was examined in the ordinary way in microscopic sections and also quantitatively analyzed by Hammar's paper method (3). The latter part of the investigation was carried out at Hammar's own laboratory. Before the investigation 1.5 gm. of connective tissue was set aside. A renewed weighing after this preparation showed the weight of the thymus as only 35.5 gm. According to Hammar's formula, $39 \times 35.5 \div 37.0$, the real weight of the thymus would then be 37.4 gm.

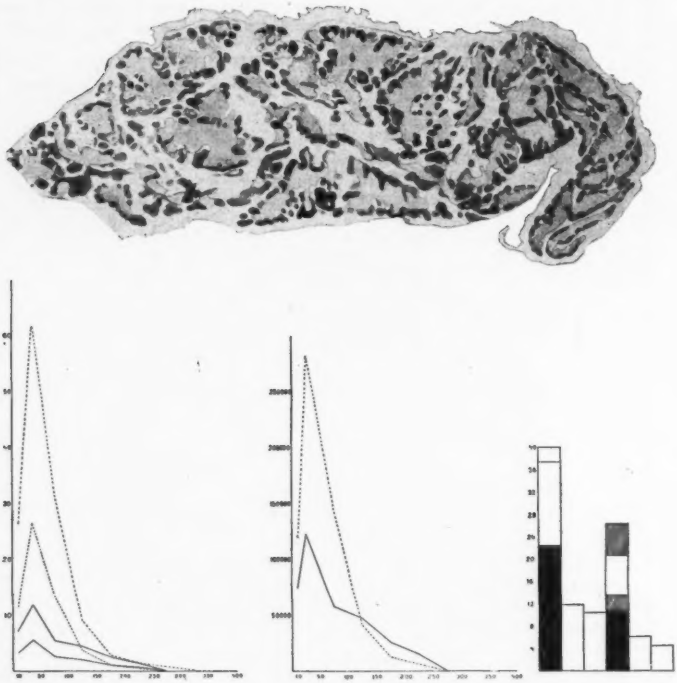


Fig. 3. Shows the relation between cortex, medulla and interstitial tissue in Case I. Cross-sections of the glands magnified 3 times. Explanation of graphs in text.

The result of the investigation is shown in Table I and Fig. 3. In this table are given, first, the figures for the two cases investigated here, and, second, for the sake of comparison, Hammar's averages and maximum and minimum values of the thymus in healthy persons belonging to the same age classes

who have suddenly died from external causes. The table records the weight of the parenchyma, the cortex, the medulla, and the interstitial tissue as well as the relation between cortex and medulla. The number of Hassall's corpuscles per mg. parenchyma and per mg. medulla and the absolute number of such formations in the whole organ are included. The Hassall's corpuscles are divided into 8 groups of magnitude, including within their limits corpuscles of a diameter of 10-25 μ for group I, 25-50 μ for group II, 50-100 μ for group III, 100-150 μ for group IV, 150-200 μ for group V, 200-300 μ for group VI, 300-400 μ for group VII, 400-500 μ for group VIII. Finally, figures are given to show the relation between groups I and II and the number of calcified Hassall's corpuscles per mg. parenchyma and per mg. medulla and in the whole organ. The data are shown graphically in Fig. 3. The left curves show the number of Hassall's corpuscles per mg. of parenchyma and medulla and the right curves the absolute number of these corpuscles. The abscissae give the size of the Hassall's corpuscles and the ordinates their number per mg. of parenchyma and medulla and in the whole organ. The complete lines denote the case in question, the hatched lines Hammar's average values for a corresponding age. Of the curves at the left the upper denote the Hassall's corpuscles per mg. of medulla, the lower, the corresponding numbers for the parenchyma as a whole. The diagram at the right shows the weight of the organ as a whole and the weights of the different components in it. The three columns at the left in the diagram refer to the case described in this paper and indicate, from left to right, the weight of the whole thymus body, the cortex and the medulla respectively. The numbers of the ordinates denote grams. In the column that shows the weight of the organ the part of the column that gives the weight of the interstitial tissue is empty. The three columns farthest to the right show in a corresponding way Hammar's average values for a corresponding age and also the maximum values for the parenchyma and the entire weight of the organ. These latter values are shown by the hatched parts of the columns and are given so as to show how far the maximum values of the case under discussion exceed Hammar's maximum values both as to the entire organ and as to parenchyma.

Direct microscopic investigation showed a very distinct boundary between medulla and cortex. Between the lobuli was seen a fairly abundant interstitial tissue consisting mostly of fat cells. The veins running in this tissue showed no thickening of the wall. The interfollicular tissue also consisted of fat cells. These mostly projected from the interlobular fat tissue in the form of wide sweeps, narrowing as they approached the medulla. In many places, however, this was not the case, but the interfollicular tissue seemed compressed and had only very narrow communication outwards; even this was sometimes absent, so that the fat cells were situated in rows between the follicles quite embedded in the parenchyma.

CASE 2. FRU MARIA BÄCK, 58 YEARS OF AGE.

The patient was admitted to the hospital on Sept. 8, 1919, and died Oct. 10, the diagnosis being *vitium organicum cordis et haemorrhagia haemisphaeri sinistri cerebri.* The patient stated that a week before admission she had had an attack of unconsciousness with simultaneous paralysis of the left side. The day before admission she had had a similar attack. Investigation at the hospital showed that the patient had hemiplegia, without aphasia, on the left side. The blood pressure was 100-110 mm. Hg. The heart showed some enlargement and a presystolic sound was heard. There were traces of albumin in the urine. The Wassermann reaction in the blood was negative. The temperature was afebrile. The pulse rate was about 70. The patient's condition remained unchanged until Oct. 10, when she suddenly became unconscious, dying within 3 to 4 minutes.

AUTOPSY REPORT NO. 358: 1919

The body length was 156 cm., the build, powerful. The weight and musculature were only slightly reduced. In general, the skin was pale in color. There was no edema.

The bones of the skull were of normal thickness and firmness. There was no osteoporosis. The brain membranes were normal. There was no arteriosclerosis in the basal brain arteries. No thrombi or emboli were visible. On the right side, in the lateral nucleus lenticularis was a red soft spot, extending out into the capsula interna and occupying in its entirety a space about the size of a walnut. The cerebellar parenchyma was otherwise of normal consistency and color.

The pericardium was smooth and shiny. Due to a right sided myocardial hypertrophy the heart was somewhat large, weighing 300 gm. The musculature was pale brownish-red and of firm consistency. There were no scars or discolored spots in it. The segments of the mitral valve were thickened and fused so that the mitral orifice could transmit only one finger. On the atrial side of one of the segments was seen the place of attachment of a loosened thrombus in the form of a rough surface the size of a hemp seed.

The lungs held air in all parts and their parenchyma was soft. The fluid that was pressed out was clear everywhere. The liver was of normal size, greyish-red in color. The stomach and intestines were normal. The kidneys were firm and dark red with a distinctly demarcated cortex. The parenchyma

showed no patches except a number of fibrous scars from healed infarcts. No fresh infarcts were observed. The spleen weighed 130 gm. The lymphatic glands were apparently not enlarged.

The ovaries showed senile atrophy. The thyroid gland weighed 30 gm. All four parathyroids were found and weighed as follows: right upper, 40; right lower, 120; left upper, 40; left lower, 370 mg. The thymus was greyish-red, large and 30 gm. in weight. The adrenals and hypophysis were preserved at the autopsy but were not weighed; when fixed the former weighed 5+5.5 gm., the latter, 695 mg.

P. A. D. *Encephalomalacia hemorrhagica capsulae internae dextrae et Endocarditis chronica cum stenose valvulae mitralis.*

Microscopic examination. Because of the hasty post-mortem examination a smaller number of organs was taken for microscopic examination in this case than in the preceding. Unfortunately, among the endocrine organs thus omitted from microscopic examination were the ovaries. The thyroid gland and adrenals appeared normal. The only thing of note is that in this case, too, the adrenals showed no signs of cadaverous softening. A transverse section of a rib showed no pathological changes. On the other hand, the kidneys showed, besides the above mentioned scars, acute degeneration in the canals, the epithelium of which was swollen and in the lumen of which was a mass, coagulated in meshes. The same thing was observed in the cavity of Bowmann's capsule. The parenchyma showed no fatty degeneration and Weigert's fibrin stain was also negative. The capillaries in the glomeruli were filled with blood. There was no cell infiltration and no changes in the vessels. It was difficult to find hyalinized glomeruli.

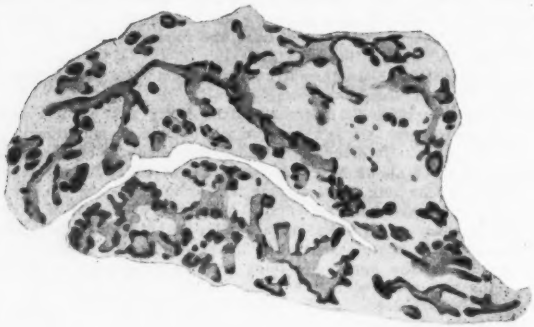
Parathyroids. The two upper parathyroids showed quite normal conditions with a moderate growth of fat between the lobuli and a moderate number of Welsh's cells. The appearance of the newly formed parenchyma and its relation to the old showed exactly the same conditions as in the preceding case. It is therefore unnecessary to repeat the description.

Thymus. The thymus was investigated in the same way as in the preceding case. The figures for the numerical investigation are given in Table I and the table is made clearer by the curves and diagrams given in Fig. 4. For the explanation of these see the description under Case I. The boundary between medulla and cortex was also very sharp in this case. The interstitial material consisted of adipose tissue. A large number of veins in this showed an extreme thickening of the adventitia. The interfollicular tissue was of the same sort as in the preceding case and showed the same curious arrangement, but it was somewhat less distinct. It may be mentioned that the sharp boundary between medulla and cortex at this age does not occur regularly in normal cases. Hammar's material, from which the figures are taken, consists of six cases, in three of which there was no distinct difference between the medulla and cortex. This is the cause of the lack of agreement apparently seen in the table between the figures for parenchyma, medulla and cortex.

DISCUSSION

Of the two cases described the first is undoubtedly the more interesting. According to the patient's statement she had suffered from frequent attacks of epilepsy. During her stay in the hospital, certainly very brief, in December, 1917, no such attacks could, however, be observed and the clinical diagnosis was neurasthenia. Nor were any epileptic fits observed during a two months' stay in the hospital a year earlier. It is thus impossible to decide whether the patient had really suffered from epilepsy. The symptoms at her death do not support the assump-

tion that she died of epilepsy. The statement in the journal as to the high frequency of the pulse and the enlarged thyroid gland of course suggest exophthalmic goiter. This would also



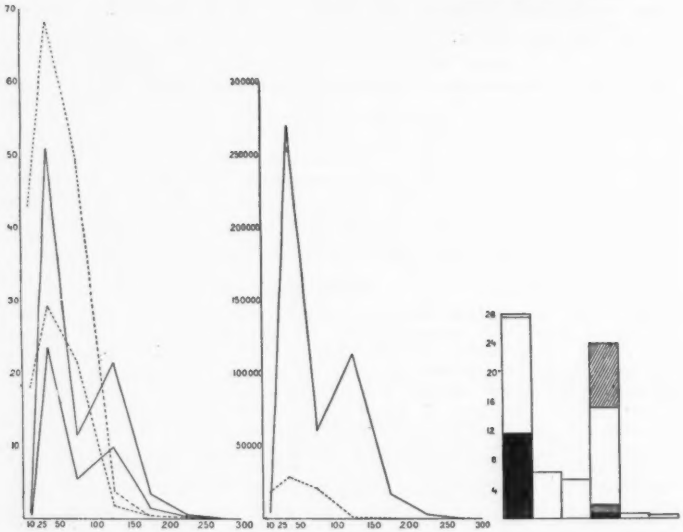


Fig. 4. Shows the relation between cortex, medulla and interstitial tissue in Case II. Cross-sections of the glands magnified 3 times. Explanation of graphs in text.

explain the manner of death. The post-mortem and the histological investigations show, however, that there was no enlargement of the thyroid gland and that this gland did not show the

features usual in exophthalmic goiter. Nor was there any enlargement of the heart. There was certainly thymus hyperplasia, but, as we shall see, it was of quite a different type from that which Hammar (4) found to be characteristic of Graves' disease. This diagnosis must, then, be rejected. As a matter of fact, neither the records of the illness nor the autopsy give any satisfactory explanation of the cause of death. The redness of the throat, the swollen tonsils, the contents of the bronchi, and the acute swollen spleen certainly indicate that, when the patient was admitted to the hospital, she was suffering from an infection in the upper air passages, but these findings do not give any explanation of the sudden death. It is noteworthy that the patient stated that during the two last years she had suffered from trouble in breathing as soon as she caught cold, especially if these statements are connected with the fact that at autopsy the lungs were found fixed in the position of inspiration. This leads one to think that the extremely enlarged thymus might have exerted compression on the trachea and the main bronchi. On further reflection, however, one must admit that such an assumption is very improbable, for the thymus is so soft and plastic an organ that it is rather improbable that it should be able to exert any considerable deforming pressure on such resistant structures as the trachea and bronchi in an adult. Nor were the contents in the bronchi of such a quantity and nature that the curious position of the lungs could be explained as due to bronchial obstruction. The only possibility left is the idea that the agonal inspirations caused the expansion of the lungs. No changes in the microscopic picture due to the expansion of the lungs can be traced.

The data as a whole indicate that the most plausible explanation of the course of the illness and the post-mortem findings is some sort of endocrine disturbance. The large thymus gland quite naturally suggests what is called status thymicolymphaticus. But, in my opinion, this term is as yet so little fixed that I shall not enter upon any discussion of the case from this point of view, but merely relate the actual conditions and the more obvious reflections to which they give rise.

First, as to the parathyroid enlargement, we must decide upon its nature. It is often difficult or impossible to distinguish

between an autonomous growth, i. e., a real tumor, and a reactive hyperplasia. This applies not least to the parathyroids, as I have had opportunity to show in a previous communication. In the present case, everything indicates an autonomous growth. It is true that two glands are enlarged, but bilateral neoplasia are not unknown in the paired human organs. Moreover, the new formation is distinctly circumscribed and unicentric, all of which strongly supports the idea of a tumor. On the other hand, the histological character of the cells of the new formation affords less evidence. The absence of fat in the cells and the lack of Welsh's cells and colloid are typical both of autonomous and reactive growth. These characteristics show only that we are concerned with young cells, which is also indicated by the fact that the parathyroids of infants have exactly this character. If we suppose that we are concerned here with an autonomous growth, which seems rather certain, and that the enlargement of the parathyroids and the hyperplasia of the thymus have really something to do with each other, then the latter must be a result of the former, because it can be supposed that hyperplasia of the thymus may possibly give rise to a reactive enlargement of the parathyroids, but not to an autonomous one. That a connection of cause and effect is really present, can of course not be proved by only two cases, but on the other hand we are so accustomed to changes in the endocrine organs being connected with one another that we certainly have some right to make an assumption of this sort. It is true that in previous cases of parathyroid enlargement I have observed, no hyperplasia of the thymus was found, nor have I been able to find any statement to this effect in the literature, but I must confess that I had not previously submitted this gland to examination according to Hammar's method and this is necessary if we are to get a reliable view as to its condition.

I pass now to an analysis of the thymus. Here it is of the greatest interest to make a comparison with the discoveries made by Hammar in his investigation of hyperplastic thymus glands in exophthalmic goiter.

In the case described we have a very extreme increase both of medulla and of cortex. The figures are more than double the average weight for a corresponding age and are considerably

above the maximum values. The weights of the parenchyma may thus without hesitation be described as above normal. We must note that Hammar's normal values are based on material derived from healthy persons who died suddenly from external causes. The deviations with regard to the weight of the thymus that others report all tend towards values less than those given by Hammar. It is thus certain that we have here a supranormal parenchyma value. The increase in the cortex and medulla was parallel. The value for the medulla is comparatively high and consequently we have a low index, which is now, however, below the limit for the normal. Here we find the first deviation from the hyperplastic exophthalmic thymus in which, in typical cases without secondary accidental involution, the cortex has the greatest share in the increase and consequently, we get a high index. Hassall's corpuscles show, for the four lowest orders of magnitude, subnormal values per mg. parenchyma and medulla. The deviation is very great. If we turn to the absolute values we find that they lie within the normal limits and in such a way that the lower orders of magnitude approach the lower limit while the higher orders reach and even exceed the upper limit. Thus the Hassall's corpuscles have not followed the increase of the other components of the parenchyma in the thymus. But further, to judge from the low values for the small Hassall corpuscles, it even looks as if there was a deficient new formation of such corpuscles. Quite opposite conditions prevail in exophthalmic goiter, for there, according to Hammar, we get supranormal total values, supranormal or at least high values per mg. of parenchyma and medulla respectively, and a surplus in the lower orders of magnitude.

In his above mentioned work on exophthalmic goiter Hammar discusses in detail the question as to whether a hyperplasia or a possible subinvolution can be considered as being present here with regard to the supranormal glands. The weight of the parenchyma gives no certain fixed points nor do the absolute numbers of the Hassall corpuscles, for they are within the normal values for the thymus at puberty, of which we have not sufficient knowledge. The occurrence of sclerotic veins in the interstitial tissue and the arrangement of the interfollicular fat cells is considered by Hammar to indicate that we are concerned

with hyperplasia in what was previously an involution thymus. He does not finally reject, however, the possibility of a subinvolution. The same is true in this case. The very high parenchyma value does not exceed Hammar's maximum value for the age 16-20, which for the entire parenchyma is 22 gm. Nor is the amount of interstitial tissue sufficient to indicate a previous greater development in an involution organ. On the other hand, this tissue is so prominent that it is impossible that we have a persistent juvenile thymus. When I use the expression thymus hyperplasia above in reference to the case described here this is thus only an expression of my subjective view. A "thymus persistens" may be present. In this case it offers the peculiarity that not all the components of the parenchyma "persist." The Hassall's corpuscles are of course, as we have seen, quite reduced to values that are very considerably subnormal for this age. The veins of the interstitial tissue do not show the above mentioned sclerotic feature the most prominent microscopic characteristic of which is an extreme thickening of the adventitia. On the other hand one sees clearly the curious arrangement of the interfollicular fat cells, for these lie, as we have seen, in rows either enclosed in the parenchyma or with a very narrow communication with the interlobular tissue. The interlobular adipose tissue normally projects on a broad basis in between the follicles. As in the thymus in exophthalmic goiter, so here, too, we get an impression that the interfollicular adipose tissue has been squeezed together by the growing follicles.

Of the cases of supranormal thymus glands investigated by Hammar and his school the case mentioned here resembles most one that Hammar (5) has mentioned in a work on the so-called thymic death. This was a case of a 23 year old man who, after having been quite healthy, jumped out of his bed one morning and fell dead. The post-mortem showed bronchopneumonia in the earliest stage and the diagnosis was "lymphatismus." Both my case and Hammar's, on the other hand, undeniably show a certain similarity to a number of cases described in literature under the diagnosis, status thymicolymphaticus. In the above mentioned case there was a supranormal parenchyma value of 16.51 gm.; the relation between

cortex and medulla gave a low index of 0.9; the Hassall corpuscles showed low absolute values and low values per mg. of parenchyma, though this applied only to the lowest groups of size. Hammar draws from this the conclusion that the Hassall corpuscles have decreased their reformation while they continue to grow. The top of the curve was displaced to group III.

SUMMARY

In a 22 year old woman with a curious and unexplained record of illness, who suddenly died, there was found, besides slight signs of an infection in the air passages, two parathyroid glands showing extreme enlargement, due most probably to autonomous growth. The thymus showed a similar extreme enlargement caused by a supranormal amount of parenchyma and interstitial tissue quite different from that of the juvenile type. It was probably a hyperplastic, not a subinvoluted thymus of puberty. It differed from the hyperplastic thymus in exophthalmic goiter in that only the values for cortex and medulla were supranormal, while the total number of Hassall's corpuscles was considerably lower than normal for a corresponding age. There was probably not only a relative but also an absolute decrease in the new formations of Hassall's corpuscles. There was a striking similarity to the thymus in a case of "lymphatismus" described by Hammar. The case affords further support of Hammar's theory that the different components in the thymic parenchyma may independently vary in amount.

In a 58 year old woman, who had an attack of hemiplegia and died about a month later from a second attack, the two lower parathyroids showed enlargement due in all probability to autonomous tumor growth. The thymus gland was markedly enlarged with a parenchyma value more than 10 times the normal. As in the preceding cases the thymus was taken to be hyperplastic, not subinvoluted. All the parenchyma components were increased, cortex and medulla to the same degree, but the Hassall's corpuscles to a smaller extent. The values for the Hassall's corpuscles per mg. parenchyma and medulla, respectively, were therefore low. In spite of the differences between them, the cases fall in a sharply defined group in which the hyperplastic thymus differs from that of exophthalmic goiter.

BIBLIOGRAPHY

1. Bergstrand, H.: Zur normalen Anatomie der Glandula parathyreoidea. Acta med. Scand. (Stockholm), 1919, **52**, 791. Literature.
2. Bergstrand, H.: Über Tumoren und hyperplastische Zustände der Nebenschildrüsen. Ibid., 1921, **54**, 539. Literature.
3. Hammer, J. A.: Methode, die Menge der Rinde und das Marks der Thymus sowie der Anzahl und Grösse der Hassalschen Körper zahlenmässig festzustellen. Ztschr. f. ang. Anat. [etc.] (Berl.), 1917, **1**, 311.
4. Hammar, J. A.: Mikroskopische Analyse der Thymus in 25 Fällen Basedow'schen Krankheit. Beitr. z. klin. Chir. (Tübing.), 1917, **104**, 469. Literature.
5. Hammar, J. A.: Mikroskopische Analyse der Thymus in 19 Fällen sogenannten Thymustodes. Ztschr. f. Kinderh. (Berl.), 1915, **13**, 153.
6. Hammar, J. A.: The new views as to the morphology of the thymus gland and their bearing on the problem of the function of the thymus. This Journal, 1921, **5**, 543-572.

SOME OBSERVATIONS ON THE NATURE AND DIAGNOSTIC SIGNIFICANCE OF THE WHITE LINE OF SERGENT ("LIGNE BLANCHE SURRENALE")

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LITERATURE

"La ligne blanche surrénale"—the white line of adrenal insufficiency was first described by Sergent (1) in 1903. Since that date considerable literature of a very conflicting nature has sprung up regarding it. During the period that has elapsed, important changes have been made in our views of the physiology of the adrenal glands and many of the older conceptions of the functions of these organs have been profoundly modified. In the light of these facts, it was thought that a systematic study of the nature and significance of the white line of Sergent would be of interest.

If the skin of the abdomen in a suitable individual be lightly stroked with some round smooth object, it is found that after a definite latent period a white line appears which gradually increases in intensity and definiteness. It persists for a minute or longer and then slowly fades. This phenomenon was first noted quite accidentally in a patient in whom a diagnosis of meningeal irritation had been made. The involvment of the adrenals was not suspected at the time, and was revealed only by the post-mortem examination which showed that the glands were almost completely destroyed by caseating tuberculous masses. On subsequent investigation Sergent found the white line constantly present in subjects showing symptoms of adrenal insufficiency.

According to Sergent cases of this condition may be classified into the following groups:

A. Pure adrenal insufficiency.
   1. Fulminating (with sudden death).
   2. Acute ("syndrome Sergent-Bernard").
   3. Sub-acute.
   4. Mild ("petite insuffisance").

B. Adrenal insufficiency with involvement of the peri-capsular nerve plexuses.
   1. Addison's disease.

The fulminating cases are of medico-legal interest only as the patient is suddenly struck down dead. Upon a post mortem examination the only lesion found is destruction of the adrenal bodies. Addison's disease, when typically present, is a well defined condition which may be recognized with some certainty. The other varieties mentioned give rise to very diverse clinical appearances as will be seen from a consideration of the symptoms.

The cardinal symptoms are arterial hypotension and asthenia of varying degrees. Digestive disturbances, such as vomiting, diarrhea, constipation, or severe abdominal pain, giving rise to a diagnosis of some acute abdominal catastrophe may be superadded. Excitement, convulsions, encephalopathy, abnormal eye signs, or coma may be present. Syncope, small pulse, tachycardia and other symptoms suggestive of circulatory disorders may be found. The clinical picture being thus so ill-defined, certain recognition of these cases becomes almost impossible in the absence of some pathognomonic sign. This, Sergent contends he has supplied, in the white line. He affirms that cases that would otherwise never have been suspected as suffering from disturbed adrenal function may by this means be readily recognized. He does not claim that the white line is present in every case of adrenal insufficiency, and admits that it may occasionally occur when the glands are functioning normally. Similar reservations must, however, be made in the case of the rose-spots in typhoid fever, but it is argued that in neither case does this detract from the diagnostic importance of the sign.

Sergent believes that adrenal insufficiency may be present as a complication in many other diseases (especially the acute infectious fevers), although no anatomical lesion of the glands can be discovered. It is suggested that the secretion, though

normally formed, is neutralized by the toxins of these diseases, and is thus unable to fulfil its normal function in the body.

In a recent publication (2) Sergent has collected most of the evidence in support of his interpretation of the significance of the white line. It is said to be a constant accompaniment of arterial hypotension, though rarely it may be elicited when the systolic pressure is higher than normal. The diastolic pressure in these latter cases is stated to be low, so that the pulse pressure is greater than usual.

All cases of Addison's disease in which the cardinal symptoms of adrenal insufficiency, asthenia and low blood pressure are present, show the white line. When melanodermia is the principal feature, the white line may not be found. The lesion is then regarded as mainly periglandular and not involving the adrenal bodies themselves.

In the various types of adrenal insufficiency, medication with whole gland or adrenin alone is said to improve the general condition. The blood pressure may rise, and then the white line can no longer be produced.

The white line is regarded as dependent on a condition of hypoadrenia. The "tonus" theory of the function of the adrenal bodies is adopted, namely, that the arterial blood pressure is maintained at its normal level by the constant secretion of the active principle of the glands. Should this be diminished in amount, hypotension results and the peripheral arterioles tend to be more dilated than usual. Light mechanical stimulation brings about constriction of these vessels; the blood supply of the corresponding area of skin is diminished and a white line is thus produced. The validity of this hypothesis will be considered later.

A number of authors have described experiences which support the views of Sergent. Among these may be mentioned Sicard (3), Bossuet (4), Siredy and Tinel (5), Paisseau and Lemaire (6), Betchov and Demole (7), and Babonneix (8).

Masselongo (9) has reported a systematic investigation on 400 patients. The white line was found in only 30 cases of this series. Of these, 22 were suffering from typhoid fever. Many cases with definite lesions of the adrenal glands did not show the white line. He thinks the sign is of considerable prognostic

value, as all the patients in whom the white line was present, died.

L. Bernard (10) obtained the white line in 31 out of 79 patients in a general hospital, i. e., almost as many patients showed the white line as did not.

As adrenal insufficiency is known to be not a very common condition, this finding appears to cast doubt on Sergent's assertions. The sign is intermittent in appearance and does not seem to bear any relation to the condition of the patient. Bernard concludes that the "ligne blanche" is not a sign of hypotension nor of adrenal insufficiency.

Masary (11) in a number of communications has come to a similar conclusion. He regards the white line simply as a "trouble vaso-moteur banal."

Timme (12) finds the white line present in the first and second stages of the pluriglandular syndrome described by him. He does not regard its association with adrenal insufficiency as proved. He states, however, that it invariably accompanies low blood pressure. It disappears quickly after a hypodermic injection of adrenin. Emotional disturbances make the eliciting of the sign impossible. In cases of Timme's syndrome, the white line can no longer be produced when the patients improve.

Professor Swale Vincent has kindly allowed me to mention that some few years ago the late Sir William Osler mentioned to him that he considered our knowledge of the cutaneous vasomotor reflexes unsatisfactory, and thought that they would repay re-examination. He suggested that it would be well to examine very carefully the evidence for the diagnostic value of the "ligne blanche surrénale."

PERSONAL OBSERVATIONS

It will be seen from the account of the literature that, though many observations have been made on subjects suffering from various morbid conditions, no thorough investigations are recorded on the normal subject.* In the absence of satisfactory control experiments, it is difficult to decide on the value which may be attached to the mass of clinical evidence which has already been accumulated.

* See final paragraph.

The subjects of the present research were a number of healthy young medical students attending the course of Physiology in this Medical School. The technique adopted was as follows. After the clinical history had been taken, the subject was placed in the recumbent position for some minutes with the abdomen free, but lightly covered. A geometrical figure was then lightly traced on the skin of the abdomen with the round smooth end of a fountain pen. The directions of Sergent were closely followed. No pressure was exerted, and no scratching occurred. The response was then noted.

The blood pressure was taken in all cases in the recumbent position with the arm at heart level. The instrument employed was an aneroid type of sphygmomanometer (Tycos). The auscultatory method of Korotkoff was used. The diastolic end point was taken as Point V of Swann, i.e., the disappearance of all sound. If 14 mm. be added to the readings given, the diastolic pressure is obtained in terms of the higher end point.

It soon became obvious, contrary to what had been expected, that many normal individuals gave a white line in response to light stroking. The white line, when present, varied widely in intensity and definiteness, and also depended, in a manner to be described, on the strength of stimulus employed.

Sergent (13) has given certain criteria of the "true" ligne blanche surrénale. This line appears after a definite latent period; it lasts for one minute or longer; it appears gradually, slowly intensifies and finally fades; it is not preceded, accompanied or followed by any red lines whatever. No response was accepted as positive unless it showed all the features detailed.

For purposes of description, it was thought advisable to define two main grades of response.

1. Marked (++) in which the line was perfectly definite, and could be seen with great ease. The edges were clear cut.
2. Definite (+) in which the line could not be seen so easily, or was brought out only on carefully shading the skin. The outline was not so sharp.

A third group in which the response was negative was also recognized. It comprised those individuals in whom the white

line was preceded or accompanied by a red line, in whom the white line was too indistinct to be quite certain about, or in whom no response at all could be observed.

One hundred individuals were examined and the results obtained are summarized in the accompanying table.

TABLE I

	White Line		
	Marked	Definite	Negative
Av. systolic pressure.....	130 mm.	129 mm.	132 mm.
Av. diastolic pressure....	69 mm.	70 mm.	72 mm.
Av. pulse pressure.....	61 mm.	59 mm.	60 mm.
Percentage of cases.....	27	39	34

As will be seen from the last line of the table, no fewer than 66 per cent of the normal subjects examined showed the white line. Sergent, however, insists that the true "ligne blanche surrénale" must have an "intensite vive." It is a matter of some difficulty to decide in any individual case whether this requirement is fulfilled, but even if all the cases described as "white line, definite" are excluded, there still remain 27 per cent of normal persons who give a response identical with that which is alleged to be indicative of adrenal insufficiency.

The average blood pressure, both systolic and diastolic, in the three groups corresponds very closely to one another. The average systolic blood pressure in Group I (white line, marked) was 130 mm., the range being from 150 mm. to 112 mm.; in Group II (white line, definite) 129 mm., the highest being 146 mm.* and the lowest 108 mm. In Group III (white line, negative), the average was 132 mm., the pressures lying between 158 and 112 mm.

The diastolic pressure figures are equally striking. In Group I, the average was 69 mm. and the range 90-60 mm.; in Group II, 70 mm. and 80-55 mm.; in Group III, 72 mm. and 90-65 mm.

There does not, therefore, appear to be any relation between the height of the blood pressure and the intensity of the white line. Many individuals with high systolic or high diastolic

* In one neurotic subject it was 175 mm.

pressures gave very marked reactions, while some with low pressures gave negative responses.

Some observations of Ravaut and Kronulitsky (14) confirm the view expressed above, though the authors themselves interpret their results differently. In 75 normal subjects the white line was definitely present in 27, a red line being obtained in the other 48 cases. The blood pressure was not taken. The authors consider the evidence, anatomical, clinical and therapeutic, conclusively in favor of the diagnostic importance of the white line, and consequently regard the 27 cases as instances of mild suprarenal insufficiency. In view of the results obtained in the present investigation, it would appear safer to argue that the white line is a phenomenon having no pathological significance, rather than assume that over one-third of apparently normal individuals are suffering from an admittedly rare condition like adrenal insufficiency.

OTHER "WHITE LINES"

A careful examination of the literature shows that a number of physiological responses have been described which bear a close resemblance to the phenomenon of Sergent. It will be useful to refer to them in this place and discuss their significance.

As long ago as 1875 Vulpian (15) described a white line which could be seen in normal individuals after lightly stroking any region of the skin "à condition que l'excitation ne soit pas très energétique." He quotes Bäumler (16) (1873) to the effect that this line can be obtained in the first stage of "typhus exanthématique" and that "la facilité avec laquelle on provoque alors le production de ces trainées blanches le porte a penser que l'excitation des artères serait plutôt augmentée que diminuée dans ces conditions morbides."

A "ligne blanche physiologique" was described by Duval (17) in 1885. The technique employed was not, however, identical with that of Sergent. The latter admits that this "ligne blanche" can be obtained in normal subjects, especially on the back of the hand and on the cheek, but maintains that it is *never* to be seen on the skin of the abdomen. It is only the pathological white line which is found in this region. The results of the present research do not support these statements of Sergent.

Hallion and Laignel-Lavastine (18) describe a "tache blanche" which is produced in normal individuals by pressing heavily on the dorsal surface of an interosseous space until the skin is completely blanched. They timed the duration of the pallor and employed it as a test of the activity of the circulation. It bears no relation to the line of Sergent.

L. R. Müller (19) has made an extensive study of the various types of dermographism and their significance. He has obtained a white line (dermographia alba) on superficial stroking in many normal young individuals, especially those with dark skins. After the age of 45, this response is less commonly obtained. The line was best marked in patients with certain nervous diseases, i e., tabes, disseminated sclerosis, transverse myelitis (on the paralyzed side of the body). He appears to be unaware of the work of Sergent, but his technique is identical in all essential features. He thinks it questionable if this "dermographia alba" has any diagnostic significance.

Cotton, Slade and Lewis (20) have repeated and confirmed Müller's observations. The subjects in their case were soldiers in a military hospital who were suffering from disordered action of the heart.

Reference may be made at this point to the work of Tracy (21). This observer, from an examination of a large number of individuals, claims that the normal reaction of the skin to a mechanical stimulus is a brief vasodilation, followed by a more prolonged vasoconstriction. In some subjects one of the two components of the reaction was absent. It is argued that these differences depend on variations in the hormone content of the blood. A double innervation of the blood vessels of the skin from the sympathetic and parasympathetic is assumed. The vasodilatation is supposed to be due to activation of the parasympathetic fibres by the "Hormone X" of Eppinger and Hess ("autonomyn"), while the vasoconstriction results from stimulation of the sympathetic by adrenalin.* If both components of the reaction are present, both hormones are assumed to be present in the blood. If the vasodilation component alone is present, Hormone X or its analogues are in excess in the

* It will be noted that Sergent regarded a vasoconstriction response as indicative of *lack* of adrenin, while Tracy produces the same reaction by injecting adrenin.

blood or the hormone adrenalin (or pituitrin with similar action) is in insufficient amount to activate the sympathetic nerve-endings in the blood vessels tested. If the vasoconstriction component alone is given, the reverse condition is present.

It is also stated that the vaco-constriction part of the response can be made to reappear in subjects in whom it was previously absent by injecting adrenin. It is supposed that the sympathetic nerve endings are thus sensitized and therefore respond more readily to the mechanical stimulus.

No attention was paid in this investigation to the strength of the stimulus employed. I am unable to confirm Tracy's observations, and in any case it is very improbable that they can bear the interpretation he places on them. It must be stated that most of the theoretical assumptions made by him are entirely unsupported by any authentic evidence.*

The white line of Baumler, Vulpian and Sergent, the dermographia alba of Müller and the white tache of Lewis appear to be the same phenomenon, one of which is present quite commonly in normal, healthy persons. Contrary to the views of Sergent, one must conclude that the white line has no pathognomomic significance, though it is of interest to enquire more deeply into its exact nature and mode of production.

THE BLOOD VESSELS INVOLVED

It has already been noted that Sergent regarded the "white line" as an arteriole phenomenon. He believed that the mechanical stimulus produced constriction of the previously dilated arterioles, with the result that blanching of the skin was effected. Considerable evidence may however be adduced against this hypothesis.

Characteristically, the white line is limited to the area of skin stimulated and is quite sharply outlined. Müller (19) points out that this would not be the case if the blanching were due to constriction of arterioles. Each arteriole supplies an irregular area of skin and the local anemia resulting from its contraction would similarly be irregular in outline and not follow strictly the line of the stroke.

*Krogh (J. Physiol., 1920, **53**, 417) is extremely skeptical on the question of the supply of the capillaries by the autonomic nervous system. For a criticism of "Hormone X" see Swale Vincent, Endocrinol., 1917, **1**, 459.

The chief features of the white line can be readily explained if local constriction of the capillaries themselves is assumed.

The white line can be obtained almost as readily on the skin of the forearm as on the abdomen. If the arm be raised to the horizontal and the pressure in an armlet is rapidly run up to 70-80 mm. above the blood pressure of the subject (i.e., to about 200 mm. Hg), it is found, as pointed out by Cotton, Slade and Lewis (20), that the white line can still be obtained and that its time relations remain unchanged. The same holds true even if an interval of ten minutes is allowed to elapse after applying the armlet.

If the circulation is normal, blocking an arteriole empties the corresponding capillaries, because the blood previously contained within them flows on into the veins. The effect of compressing the arm in this experiment has been, however, to slow down or stop completely the flow in the vessels below the block and produce a stagnant circulation. In such a system, constriction of the *arterioles* would drive blood out of them into the capillaries and dilate them still further, as their contents could not pass on in the normal way, owing to the obstruction to the natural outflow from the veins. The blanching of the skin must therefore be due to the contraction of the *capillary* wall, which actively drives the blood out into the neighboring veins.

If a painful stimulus, such as a pin prick, be applied to the skin, a flush results, which can readily be shown to be an arteriole phenomenon. The flush spreads a variable distance from the area stimulated, is mottled in color from alternating islets of hyperemia and normal skin, and the edge is crenated, as would be expected from the manner in which an arteriole is distributed to the skin. The color is red throughout and does not tend to become purple from oxygen deficiency, proving that rapid flow of blood is occurring and not the stagnation which is typical of filled capillaries. If, over such an area of flushing, a line of light pressure be drawn, a white line appears which replaces the erythema over an area strictly limited to the zone stimulated. As pointed out by Lewis (20), we have here the characteristic line of capillary constriction, superimposed on an irregular hyperemia due to dilatation of arterioles.

It may thus be concluded that the white line is due to local emptying of the capillaries as a result of active contraction of some elements in their walls, and is quite independent of the condition of the arterioles.

FUNCTIONS OF THE CAPILLARIES

It must be admitted that this view is not in accord with orthodox teaching, which hitherto has assigned to the capillaries a purely passive part in the circulation. Recent research, physiological and clinical, seems to show that these older conceptions must be seriously modified.

Krogh (22) in a series of papers has confirmed and extended the older work of Stricker (23), Steinach and Kahn (23) and Roy and Graham-Brown (23). He has made many observations on the frog to show that the reactions of the capillaries can be independent of the simultaneous reactions of the arterioles and are always practically independent of the arterial pressure. The capillaries belonging to the same arteriole may change in diameter in opposite directions. A drop of urethane solution may dilate the capillaries to a diameter of 50 μ while the parent arteriole is so narrowed that the red corpuscles can just be squeezed through one by one. Dale and Richards (24), working with histamine, obtained a fall of blood pressure when the arterioles were contracted. They could explain their results only by assuming that histamine acted directly on the capillaries and produced this active dilatation.

Rouget (25) has described branched cells arranged outside the capillaries which he considers to be the contractile elements. His results have been confirmed by Mayer (26).

Many observations on the human subject have been made at the Tübigen Clinic. By means of the capillaroscope (Hautkapillarmikroskop of Müller-Weiss) (27) direct inspection can be made of the capillaries in man. Attention is directed chiefly to the skin at the root of the nail where the capillaries do not run vertically as elsewhere, but horizontally. The results obtained by this means are in full agreement with the conclusions of the previous workers mentioned.* In the present state of knowledge, the burden of proof appears to be, as Sir Thomas

* This work has been repeated and extended in this laboratory. The results will be published elsewhere.

Lewis (20) remarks, with those who deny any powers of active contraction to the capillaries.

RELATION OF RESPONSE TO STRENGTH OF STIMULUS

In many of the subjects, the relation of the response to the strength of the skin stimulus was investigated. When a definite white line was obtained on very superficial stroking, gradually increasing the strength of stimulation produced the following results. The line, which at first was quite distinct, with clear cut edges, became wider and more indefinite in outline; then a vague whiteness or no response at all was obtained. The next stage was a central pink tint, leading on to a definite red line which was often flanked by a white line on either side. Using the criteria discussed earlier, this red line can be shown to be due to capillary dilatation. Heavier stimulation, giving rise to actual pain, produced the arterial flush already described.

When the white line was not obtained, heavier stroking at first produced no response. On further increasing the strength of stimulation, a red line, not accompanied by white lines, resulted.

The following stages may thus be recognized in the normal vascular responses of the skin:

1. Capillary constriction (white line).
2. No visible response.
3. Capillary dilatation (red line).
4. Arterial dilatation (flush).

In a proportion of subjects, the first effect is not obtained. The red line and flush, on the other hand, are constantly present.

With all grades of stimuli, the *arterial* response of the skin appears to be vasodilatation. The *capillaries,* however, respond differently to weak and strong stimuli, a weak stimulus producing constriction, a strong stimulus, dilatation. The central red line of the red and white reaction, mentioned above, is thus due to the heavy stimulus over the line of the stroke, the bordering white lines resulting from the weaker stimulus where only slight stretching of skin is occurring. An analogy may be drawn to the arterial responses following stimulation of sensory nerves. Vincent and his co-workers (28) have shown that a weak stimulus produces a fall of blood pressure (vasodilation) while a strong stimulus results in a rise (vasoconstriction).

A POSSIBLE NERVOUS MECHANISM

It is improbable that the capillary reflexes are carried out through the central nervous system, because of the accurate way in which the reaction is limited to the area stroked. Müller believes that they are due to direct stimulation of the capillary wall—heavy stroking paralyzing the contractile elements with consequent dilatation, a lighter stroke producing contraction. Krogh (29), from his experiments in the frog, agrees that they are not true reflexes because they are unaffected by section of the nerves to the part. The response to local stimulation is, however, abolished on the application of cocaine, and he is therefore inclined to the view that they are axon reflexes. The sensory nerves divide to provide the capillaries (and arteries) with vasodilator fibres and to supply sensory nerve endings which are capable of responding readily to mechanical stimuli. Other nerves and nerve endings (with an even lower threshold value) may be responsible for capillary constriction. In subjects not giving the white line, the two opposing effects would appear to neutralize one another, until a certain grade of stimulation is attained. It should be noted, however, that Langley (30) does not regard the nerve supply of the capillaries as definitely proved.

THE SYNDROME OF ADRENAL INSUFFICIENCY

Modern experimental work has shown that the tonus theory of adrenal function must be abandoned. The evidence will be found fully discussed in the papers of Swale Vincent (31) and Stewart (32). Sergent himself in a recent communication acknowledges that the normal blood pressure is not maintained by adrenin, and presumably he would be prepared to modify his original explanation of the mechanism of the production of the white line. It has been shown above that the white line is a capillary, not an arteriole, phenomenon, and there is no available proof that adrenin has any action on the capillaries. The investigation on 100 healthy men demonstrated that the line is a physiological occurrence. This view is supported by the work of the other authors who have been quoted.

Since the foregoing was written my attention has been drawn to a paper by Kay and Brock (33), who have investigated the clinical significance of the white line. They agree that the

response bears no relation to adrenal gland activity. They find it frequently present in normal subjects (especially young adults), and it bears no relation to the blood pressure. It can be made to appear in the face of an injection of adrenalin given subcutaneously. These authors do not discuss the exact physiological mechanism of the response but appear to regard with favor Tracy's theory that it is a manifestation of sympathetico-tonia.

The position of the syndrome of adrenal insufficiency must therefore be reconsidered.

If the adrenals are completely extirpated in an animal, death results after a short period. The symptoms observed agree fairly closely with those noted in the human subject in whom complete destruction of the glands has actually occurred. If, however, a small portion of the glands be retained in the experimental animal, no ill effects whatever seem to result. The conception of *mild* suprarenal insufficiency thus receives little support from the physiological side. The human post mortem evidence is likewise too meagre to place this condition on a firm pathological basis. Diagnosis of these cases has been based on the insecure foundation of tests like the white line or the response to medication with suprarenal products. It is suggestive that equally effective cures are claimed for adrenin alone as for extracts of the whole gland. It must be remembered, too, that the symptoms of adrenal insufficiency would be those arising from a disturbance of *all* the functions of the glands; in most of the clinical records, however, there is an attempt to correlate the symptoms with the supposed functions of the medulla only.

It would appear from the foregoing that it is premature to attempt to recognize clinically a condition of mild suprarenal insufficiency until our knowledge of the part played by the adrenals in the normal body economy is considerably extended.

SUMMARY

1. The white line of Sergent is described and the literature of the subject is reviewed.

2. It is shown by an investigation of 100 healthy individuals that the white line is a phenomenon occurring in a large proportion of normal subjects and is without pathological significance.

3. A number of analogous physiological responses are described.

4. The white line is not related to adrenal insufficiency nor to abnormally low systolic or diastolic pressure.

5. The white line is produced by local emptying of the capillaries due to the active contraction of some elements in their walls, and is quite independent of the condition of the arterioles.

6. A nervous mechanism of the nature of an axon reflex may be involved.

7. The bearing of this investigation on the clinical recognition of adrenal insufficiency is discussed.

I must thank Professor Swale Vincent for his kindly encouragement and advice throughout this investigation.

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BIBLIOGRAPHY

1. Sergent, E.: Presse méd (Par.), 1903, **11**, 813-815.
2. Sergent, E.: Etudes cliniques sur l'insuffisance surrénale. Paris, 1921.
3. Sicard: Bull. et mem. Soc. méd. d. hop. de Par., 1904, 3. s., **21**, 848-852.
4. Bossuet, G.: Gaz. hebd. d. sc. méd. de Bordeaux, 1905, **26**, 469-472.
5. Siredey, A. & Tinel: Bull. et. mem. Soc. méd. d. hop. de Par., 1907, 3. s., **26**, 145.
6. Paisseau, G. & Lemaire, H.: Presse méd. (Par.), 1916, **24**, 468.
7. Betchov, N. & Demole, V.: Rev. méd. de la Suisse Rom. (Genève), 1918, **38**, 379.
8. Babonneix, L.: Monde méd. (Par.), 1917, **27**, 167.
9. Massolongo: Abst., Lancet (Lond.), 1918, **11**, 713.
10. Bernard, L.: Tribune méd. (Par.), 1907, n. s., **39**, 453.
11. de Masary, E.: Bull. et. mem. Soc. méd. d. hop. de Par., 1907, 3. s., **24**, 1385-1391.
12. Timme, W.: Endocrinol. (Los Angeles), 1918, **2**, 209-240.
13. Sergent, E.: Endocrinol. (Los Angeles), 1917, **1**, 18-23.
14. Ravaut, P. & Krolunitsky, G.: Bull. et mem. Soc. méd. d. hop. de Par., 1914, 3. s., **39**, 624-629.
15. Vulpian: Leçons sur l'appareil vasomoteur. Paris, 1875.
16. Bäumler: Quoted from Müller, L. R. (19).
17. Duval: Quoted from Sergent, E. (2).
18. Hallion & Laignel-Lavastine: Bull. et mem. Soc. méd. d. hop. de Par., 1903, 3. s., **20**, 133-142.
19. Müller, L. R.: Deutsche Ztschr. f. Nervenh. (Leipz.), 1913, **47-48**, 413.
20. Cotton, T. F., Slade, J. G. & Lewis, T.: Heart (Lond.), 1917, **6**, 223.
21. Tracy, E. A.: Boston M. & S. J., 1916, **175**, 197.
22. Krogh, A.: J. Physiol., 1919, **52**, 470.
23. Stricker, Steinach, Kahn, Roy & Brown: Quoted from Krogh (22).
24. Dale, H. H. & Richards, A. N.: J. Physiol., 1918, **52**, 110.
25. Rouget: Compt. rend. Acad. d. sc. (Par.), 1879, **88**, 916.
26. Mayer: Anat. Anz. (Jena), 1902, **21**, 442.
27. Weiss, E.: Deutsches Arch. f. klin. Med. (Leipz.), 1916, **69**, 1-38.
28. Vincent, S. & Ogata, D.: J. Comp. Neurol., 1919, **30**, 355-380.
29. Krogh, A.: J. Physiol., 1920, **53**, 413.
30. Langley, J. N.: Autonomic nervous system. Cambridge, 1921.
31. Vincent, S.: Endocrinol. (Los Angeles), 1917, **1**, 140-149.
32. Stewart, G. N.: Endocrinol. (Los Angeles), 1921, **5**, 283-306.
33. Kay, W. E. & Brock, S.: Am. J. M. Sc. (Phila.), 1921, **161**, 555-561.

Table I "Ligne blanche" Marked (++)

Subject	Age	Blood Pressure			White Line		Clinical History and Present Condition
		Systolic mm.	Diastolic mm.	Pulse Pressure mm.	Latent Period, Seconds	Duration, Minutes	
H. M. J.	18	136	75	61	25	2	Good health.
F. J. T. F.	23	136	90	46	15	2	Good health.
E. V. S.	19	140	65	75	15	2	Good health.
F. E. L.	19	130	65	65	15	2½	Good health.
D. A. W.	19	124	?30	?94	20	2	Good health.
W. R. S. P.	20	125	65	60	15	2	Had "orthostatic albuminuria."
J. A. W.	23	133	75	58	15	2	Good health.
W. G. C. G.	20	126	70	56	10	2½	Good health.
F. G.	19	118	80	38	10	2	In hospital 7 years ago for "septic condition" Now quite well.
S.S.	18	150	85	65	12	2	Good health.
D. H.	21	125	80	45	10	2	Good health.
H. B. S.	20	144	70	74	15	1½	Septic tonsils.
C. E. B.	19	118	80	38	25	3	Good health.
A. M. M.	22	125	65	60	20	—	Operation for glands in neck.
D. P. G.	19	130	60	70	20	—	Good health.
A. L. B.	17	140	—	—	10	3	Good health.
P. B. J.	20	132	72	60	12	1½	Good health.
J. W. S.	24	122	72	50	—	—	Good health.
D. C.	24	128	65	63	15	1½	Good health.
R. H. F.	20	138	65	73	15	2½	Good health.
C. R. P.	22	136	60	76	10	1	Good health.
R. W. E.	20	142	60	82	15	1½	"Strained heart."
E. W. P.	21	112	60	52	10	1½	Good health.
J. R.	26	128	70	58	12	1¼	Good health.
P. B. S.	28	126	75	51	10	2	Malaria.
J. V. D.	29	120	70	50	12	1½	Good health.
S. W.	23	118	75	43	10	1½	Good health.
Average.....		130	69	61			

Percentage of Cases, 27.

Table II "Ligne blanche" definite (+)

Subject	Age	Blood Pressure			Clinical History and Present Condition
		Systolic	Diastolic	Pulse	
T. A. B.	18	132	80	52	Good health.
W. H. G.	19	132	55	77	Good health.
Z. R.	22	108	80	28	Good health.
A. L. H.	24	130	65	65	Good health.
A. D. B.	20	126	85	41	Good health.
K. S. S.	21	136	80	56	Appendicitis 1915. Irritable heart.
A. T. G.	25	114	85	29	Hist. of syst. murmur at apex. Now nor.
F. E. T.	22	128	65	63	Good health.
L. B.	24	132	80	52	Good health.
J. R. T.	21	136	70	66	Good health.
P. R. P.	21	138	70	68	Good health.
D. S. D.	19	128	65	63	Good health.
G. W. A.	22	142	70	72	Neurasthenia.
A. W.	21	122	60	62	Good health.
E. J. A.	23	122	65	57	Good health.
D. R. S.	21	138	65	63	Good health.
W. G.	25	132	75	57	Good health.
D. J. H.	22	132	70	62	Good health.
L. R.	18	136	70	66	Good health.
H. W. G.	23	122	70	52	Good health.
W. L. B.	21	118	64	54	Nephritis at 2.
H. I. D.	22	142	70	72	Good health.
E. E. B.	18	130	80	50	Good health.
H. L. P.	27	108	65	43	Good health.
S. S. B.	23	116	70	46	Good health.
J. F.	21	140	70	70	Good health.
W. F.	22	128	70	58	Good health.
S. W.	22	125	60	65	Good health.
M. R. S.	24	146	70	76	Good health.
F. R. L.	17	121	65	56	Good health.
M. B. W.	25	134	70	64	Good health.
H. D. P.	22	122	80	42	Good health.
G. H. T.	23	136	65	71	Good health.
W. M. B.	24	138	70	68	Good health.
C. A. B.	26	126	70	56	Good health.
T. E. E.	25	122	70	52	Pneumonia 3 years ago.
A. P. M.	26	124	60	64	Good health.
G. V. G.	25	175	65	115	Tachycardia, pulse 130, neurotic, sweats.
D. E. B.	26	126	75	51	Good health.
Average.....		129	70	59	

Percentage of Cases, 39.

Table III "Ligne blanche" negative

Subject	Age	Blood Pressure			Clinical History and Present Condition
		Systolic	Diastolic	Pulse	
E. A. D.	19	118	70	48	Good health.
E. J. S.	21	128	90	38	Good health.
F. D. M. H.	22	138	80	58	Good health.
G. S.	21	136	75	61	Goos health.
A. G. S.	20	130	80	50	Good health.
S. W. A.	25	126	70	56	Good health.
C. G. U. C.	18	128	70	58	Good health.
J. S. R. J.	23	146	70	76	Good health.
H. H.	25	128	65	63	"Emphysema."
C. A. M.	23	112	65	47	Good health.
E. D. T.	26	128	65	63	Good health.
R. J. N. C.	20	125	70	55	Good health.
J. D. R. M.	22	138	65	73	Good health.
J. B.	23	135	65	70	Good health.
W. G. D.	28	142	75	67	Good health.
M. B.	23	158	80	78	Good health.
P. R. P.	20	125	70	55	Good health.
E. O. L.	23	122	80	42	Good health.
S. G. S.	25	128	65	63	Good health.
H. G. L. F.	24	116	65	51	Good health.
G. S. S.	20	114	65	49	Good health.
C. F.	22	148	70	78	Good health.
J. W.	20	126	70	56	Good health.
P. J. M.	22	146	75	71	Good health.
D. B. M.	26	146	85	61	Good health.
L. E. M.	24	142	70	72	Good health.
F. H. A.	26	148	80	68	Good health.
D. E. T.	40	132	70	62	Good health.
L. H. R.	29	124	70	54	Good health.
H. H. J.	23	126	65	61	Good health.
F. W. C.	21	126	80	46	Good health.
A. T. F.	23	128	80	48	Good health.
A. F. D.	23	142	65	77	Wound of kidney. Large abdominal scar.
Average.....		132	72	60	

Percentage of Cases, 34.

THE RELATION OF THE ADRENALS TO MUSCULAR ACTIVITY.*

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That the adrenals bear some direct relation to muscular activity has been known for many years. One of the earliest recognized symptoms of adrenal insufficiency was muscular asthenia. This is undoubtedly the most characteristic symptom. In Addison's disease and in experimental insufficiency the loss of muscular power is very striking. Individuals previously quite strong become weak and easily fatigued.

After the discovery of epinephrin it was shown that this substance could benefit fatigued muscle (1). This suggested the possible rôle of the adrenals in muscular exercise. No one so far as we know, however, has demonstrated that there is an increase in epinephrin output during exercise. Stewart and Rogoff (2), without attempting to show any difference in epinephrin output from exercise, did not observe any difference between the working power of normal cats and those with a large portion of the adrenal tissue removed and in some instances the remaining fragment denervated.

We have studied the influence of exercise in fifty cats by means of a treadmill (3), most of them for at least a few weeks and a smaller number for considerably more than a year. Our results point to a very definite relation between epinephrin output and muscular response.

We have used the denervated pupil as a test for epinephrin. By its means we are able to recognize increases in the epinephrin output at any stage of exercise without recourse to operative procedures. That epinephrin is responsible for dilatation of the denervated pupil during exercise has been shown by denervation of the adrenals in animals which gave the reaction, after which dilatation was abolished. We have proved that such dila-

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tation is not due to central nervous influence, by removal of the ciliary ganglion as well as the superior cervical ganglion. In the five cats in which this operation has been performed exercise in the treadmill has easily elicited dilatation of the denervated pupil. Abolition of dilatation of the pupil following complete adrenal ablation in cats with the superior cervical ganglion removed and the response of a completely denervated iris with adrenals intact, are conclusive evidence that the dilatation of a denervated pupil during exercise must be due to something from the adrenals. Epinephrin, being the only substance in the adrenals known to possess this power, must be responsible for the dilatation of a denervated pupil from exercise.

All exercise is usually accompanied by some increase in the epinephrin output. But the extent of the increase is determined by the intensity and duration of the activity. Judging from the dilatation of the denervated pupil, the epinephrin is released in gradually increasing quantities during vigorous exercise. Hard fast work will develop the maximal output much earlier than will moderate activity. Two cats were led around the room at a moderate pace; one trotted along willingly, the other slid and held back. The former performed more work and gave evidence of a small increase in the epinephrin output at 51 meters, the denervated pupil being just larger than the control. The epinephrin output was maintained at about this level for the whole period of 544 meters, there being no further increase. Upon placing the animal in the treadmill there was a further increase in the output after 57 meters had been covered. The other cat did not show an increase in the epinephrin output until it had walked more than 500 meters around the room and then it was just noticeable. Upon placing it in the mill it showed a decided increase in the epinephrin output by the time it had traveled 143 meters.

The increased epinephrin output during exercise persists for some time after cessation of work—the longer the work period, and the more intense the exercise the longer the after-secretion. An increase may persist for one or more hours in some instances after vigorous work; in others it may be only a matter of a few minutes. Once the adrenals have started to secrete additional epinephrin, it is frequently very easy, after short rest periods, to obtain a very quick rise in the output.

Typical eye reactions are shown in the accompanying figure (Fig. 1).

This increase in epinephrin has an important bearing on muscular efficiency.

THE RELATION OF EPINEPHRIN TO THE WORK PERFORMED

We have observed that an animal can travel faster and go farther if there is a decided increase in the epinephrin output. Moreover, spurts of fast pacing in the mill have been accom-

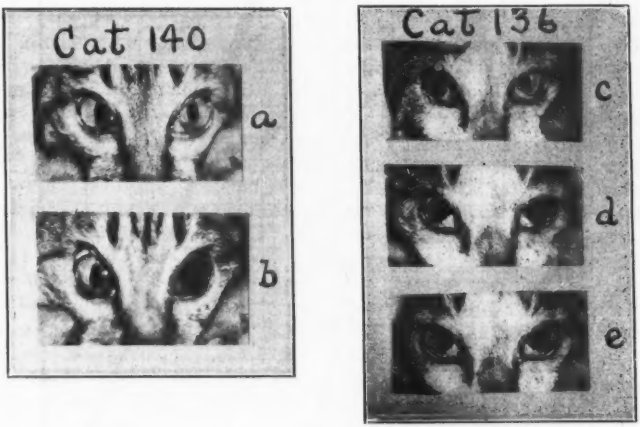

Fig. 1. Dilatation of denervated pupil from exercise. Cat's left eye denervated (superior cervical ganglion removed).. Cat 140; *a* before, *b* after travelling 153 meters in 3 min. Cat 136: *c* before, *d* after travelling 185 m. in 5 min., *e* after travelling 437 m. in 15 min.

panied by greater increases in epinephrin. Occasionally a perfectly normal animal will fail to show any epinephrin increase; then if the work is carried far enough it will often go into convulsions. However, the same animal is able to travel much farther when the usual increase in epinephrin is obtained (Fig. 2).

Animals which are not able to increase the epinephrin output on account of denervation of the adrenals, do not work so well as normally. But if the nerves are allowed to regenerate they recover this power together with the increased epinephrin output accompanying exercise.

Adrenalin injections likewise produce a beneficial effect on the work performed. Injected intramuscularly in order to prolong the absorption, 2.5 cc. of a 1:10,000 solution (into the muscles of the back) caused a cat which had already traveled 500 meters without showing "second wind" or increased epi-

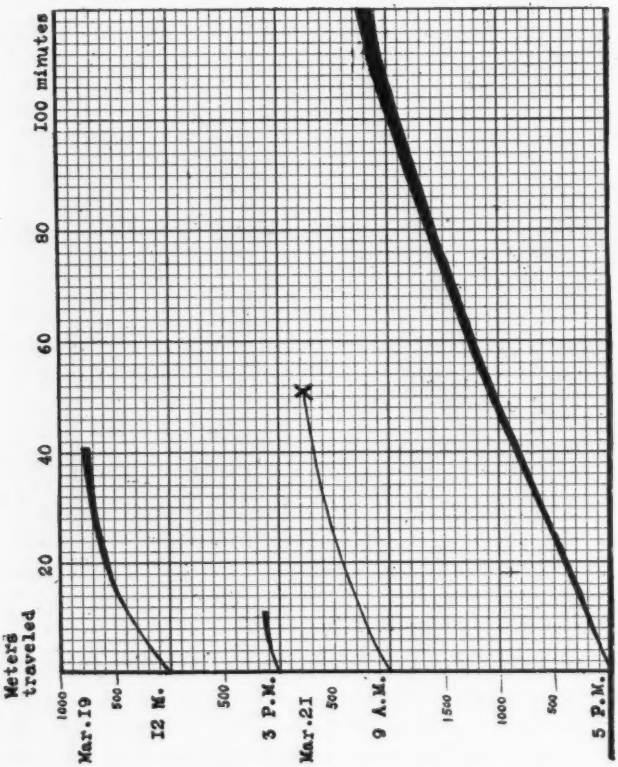

Fig. 2. Work done in treadmill by a normal cat in different tests. Increase in epinephrin output indicated by increasing the width of the line. Convulsions occurred at X.

nephrin, to improve markedly in pacing and work generally during the next 500 meters. An injection of 1 cc. of a 1:10,000 solution into another cat after it had worked more than 500 meters caused it to pace better than during the preceding period. The improvement continued until it was working better than ever before. Both cats possessed but a single adrenal, the nerves of which had been cut several months before. Regeneration had

taken place but was far from complete, so that a normal increase in the exercise output of epinephrin was sometimes difficult to obtain. The relation of epinephrin to working power is very well shown by the following examples:

Cat A. Three weeks after destruction of a part of each adrenal by cautery, testing in the treadmill for 1144 meters showed an excellent output of epinephrin (eye reaction); likewise the cat appeared to have "second wind." The cat apparently could have gone much farther. One month after removal of the right adrenal, testing in the mill showed a good increase in epinephrin, although less than in the first test; likewise the work was not so vigorous. Ten days after cauterizing the left adrenal the second time, testing in the mill showed a slight increase in epinephrin. The cat was weak but willing. On the basis of adrenal insufficiency a series of adrenalin injections were given. A total of 12.6 cc. of a 1:5,000 solution was injected into the muscles in forty-seven minutes. After a portion had been injected, the cat became more active and seemed to feel better. The denervated pupil had become markedly dilated showing that epinephrin was being absorbed. However, it should be noted that it took a great deal more adrenalin to produce the required dilatation than in a cat with normal adrenals. The cat was again tested in the treadmill, working aggressively and doing very much better than in the first test. The second time it traveled 543 meters in twenty-five minutes and felt fit at the end because it jumped out of the mill and stood up. In the first test it traveled only 240 meters, the test being stopped because of the apparent weakness.

Cat B. Operations, time of operations, and time of testing were identical with Cat A. The results were very similar in all tests. In the test following the second cauterization of the single remaining adrenal, the cat was obviously suffering from adrenal insufficiency because it had decreased in weight from 3.3 kgm. to 2.4 kgm. and appeared lethargetic. From the start of the mill, the cat appeared weak but willing. There was no evidence of an epinephrin increase. At 275 meters the cat was taken out, but it could not stand. After the injection of 4.2 cc. of 1:10,000 adrenalin solution intramuscularly in the course of fifteen minutes, the cat instead of moping listlessly became active, cleaning itself. After further injections of a total of 7.5 cc. of 1:5,000 adrenalin the cat was again placed in the treadmill. It appeared to have lost its former weakness, working much better than in the first test.

The improvement obtained from adrenalin injections resembles the "second wind" which has been observed in some of our cats. In fact our observations lead us to believe, with Cannon (4), that epinephrin plays an important part in the development of "second wind." At the time when our animals showed

this greater efficiency an increase in the pupil dilatation was usually noticed.

The possible rôle of epinephrin in "warming up" exercise is suggested by our observations. An athlete goes through a few vigorous paces and in so doing undoubtedly forces the epinephrin output to a higher level. When he is put to the test he is able to start with a higher muscular efficiency, partly on account of the extra epinephrin already released, although of course there are other factors involved.

FATIGUE CONVULSIONS

Occasionally in normal cats and frequently in certain individuals which possess adrenals with only partially regenerated nerve fibers (the nerves having been cut some time before) convulsions will develop while the cat is working in the treadmill. The animal usually lies on its side, the whole musculature undergoing spasmodic contraction. Sometimes, it moves its feet rapidly as though it were pacing and jumping in the mill. This is accompanied by great salivation and marked dilatation of the pupil. Convulsions are frequently preceded by slight muscular twitchings. They are followed by heightened irritability in some instances and by a brief prostration in others. In no instance have there been any lasting ill effects.

Convulsions occur only in certain individuals, while in others, according to our observations, they never occur. A certain amount of work must precede these seizures. Thus for some time after removal of one adrenal and denervation of the other it is impossible to obtain convulsions because the animal will not work hard. Usually, there is no dilatation of the pupil preceding convulsions; however, in two animals only, this has occurred. One adrenal had been removed, the other adrenal had been denervated several months before in each animal. In one animal the dilatation was very poorly developed; in the other, the dilatation was marked, although not as well developed as in a normal cat. In both instances, the animals traveled much farther than was possible in the earlier period. Seven months before, convulsions would begin at from 500 to 728 meters in one cat and 476 to 1020 meters in the other. Seven months after, the first cat was seized with convulsions at 945 meters,

while the second was seized with convulsions at 1461 meters. Convulsions were less common in both animals at seven months.

The relation between dilatation of the denervated pupil and convulsions is shown by the following example: A normal animal, which had been seized by convulsions at 780 meters in the morning (no epinephrin had been secreted according to the eye reaction), traveled 2240 meters without convulsions when epinephrin was secreted. The denervated pupil dilated early in the test and continued to increase in size until it became maximal (Fig. 2).

It appeared from these observations that epinephrin might prevent convulsions, therefore we tried the injection of adrenalin. Instead of decreasing the occurrence and postponing the onset, adrenalin seemed to increase the occurrence and hasten the onset. We tested four cats, three of which had previously been seized by convulsions. In all three, convulsions occurred earlier than normal. In the fourth, no convulsions developed. In every instance the animal worked hard in the treadmill before convulsions appeared. One of the cats serves as an illustration. This cat, a normal one (3.44 kgm.) had been seized by convulsions the first time it had been tested in the treadmill, but had failed to be affected in succeeding tests. Two doses of adrenalin were injected into the muscles of the back. The first was 0.5 cc. of a 1:2,000 concentration. The second one, 1.5 cc. of a 1:5,000 concentration, was given after the cat had traveled 400 meters. Following the second dose, the animal was "full of fight." Upon being placed in the treadmill it paced, until stopped by convulsions, 572 meters in eleven minutes. This was certainly faster and a longer continuous pacing than was ever obtained before in this cat. Moreover, before the second injection of adrenalin the cat had not paced more than three meters at a stretch.

Adrenalin, therefore, does not prevent convulsions. On the other hand we are not in position to say that epinephrin causes convulsions. Benedek (5) was able by the injection of epinephrin to cause typical seizures in seven patients out of nineteen, who were subject to epilepsy. Yet one cannot say that epinephrin is the cause of epilepsy.

SUMMARY

1. In normal animals, except in rare instances, there is an increase in the output of epinephrin accompanying exercise. This increase is greater, the more vigorous and the more prolonged the exercise.

2. The increased output of epinephrin persists for some time after the exercise ceases, the duration of the increase depending to some extent upon the amount of work performed.

3. Injections (intramuscular) of adrenalin improve the output of work in many normal cats and in cats with epinephrin deficiency.

4. An animal can go farther and travel faster when there is an increase in the epinephrin output during exercise.

5. Epinephrin may hasten the onset of convulsions due to exercise.

BIBLIOGRAPHY

1. Gruber: This Journal, 1919, **3**, 145.
2. Stewart & Rogoff: J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 87.
3. Hartman, Waite & Powell: Am. J. Physiol., 1922, **60**, 255. Also unpublished work.
4. Cannon: Bodily Changes in Pain, Hunger, Fear and Rage. N. Y., 1915, D. Appleton & Co.
5. Benedek: Wiener klin Wchnschr., 1918, **31**, 1365.

A CASE OF SPONTANEOUS DISAPPEARANCE OF DIABETES

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In a previous communication (1) two cases of thyroid diabetes were reported. In these cases the glycosuria disappeared after the removal of a portion of the thyroid gland. Of the cases then reported, the second is still under observation and is still sugar free on a very liberal diet.

Since the publication of the article referred to, Friedman (2) and his co-workers have announced, and in part published, the results of animal experiments which have a very direct bearing on the question under consideration. These investigators found that if dogs were depancreatized and thus rendered diabetic, the diabetes could be rendered less severe by ligation of all of the vessels of the thyroid and that the glycosuria could be caused to disappear by the subsequent removal of that gland. This very brief summary fails to do justice to the many interesting observations made by Friedman, whose original papers should be consulted for the details.

A Russian Hebrew, female, married, aged 45 years, came under observation with the following history: A maternal aunt was said to have had diabetes. The patient recalled the usual diseases of childhood. She was married at 19 years and had five children, all alive and well. At the age of 30 she had applied for life insurance and had been rejected because sugar was found in the urine. This was her first intimation that she had diabetes. Following this she subjected herself to medical treatment, but was never sugar free, and during treatment she developed the clinical symptoms of thirst, itching and polyuria. In seven years she lost 35 pounds. At the age of 40 a stormy menopause occurred. Three years before her death, with subsidence of the menopause symptoms, repeated examinations of the urine failed to show sugar and she was able to eat candy without having glucose appear in the urine. Two years before death she noted a boggy swelling of the hands and limbs, a

general harshness of the skin, and a slowly increasing dyspnoea accompanied by attacks of vertigo. Members of her family noted mental deterioration. At that time physical examination showed a cardiac hypertrophy with a systolic murmur at the apex. The subcutaneous tissues were generally boggy and the systolic blood pressure varied from 190 to 240 mm. Hg. The urine contained 3.5 gms. of albumen per liter and there were numerous casts. She did not respond to treatment and died in coma of supposedly nephritic origin.

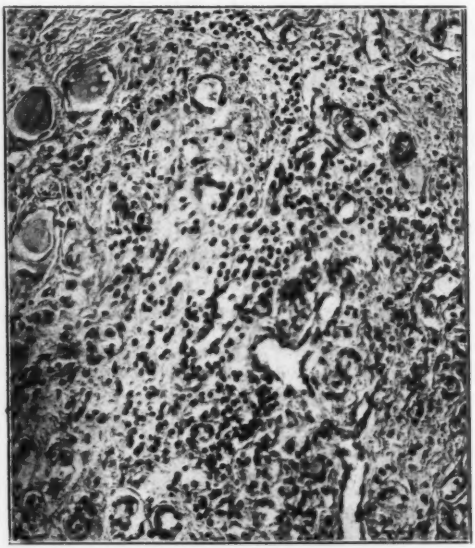

Fig. 1. Section of fibrotic thyroid x 200.

At the autopsy several interesting lesions were found. Those not bearing directly on the subject in hand were: hypertrophied cardiac muscle with relative valvular insufficiency; marked chronic interstitial nephritis; post-mortem cystic degeneration of the adrenals; fibrotic ovaries; and diffuse arteriosclerosis, most marked in the aorta.

The lesions of particular interest were found in the pancreas and thyroid. The thyroid gland (Fig. 1) showed almost complete destruction of the secreting alveoli and their replace-

ment by connective tissue richly infiltrated with round cells. The pancreas showed a variety of lesions. In the general region of the head there was marked fibrosis, most of the glandular elements being destroyed and only an occasional island of Langerhans persisting. In the body of the organ the outstanding histological lesion was marked hypertrophy of the islands of Langerhans, most of these structures being three to four times their usual size (Fig. 2). The tail of the pancreas showed no noteworthy change.

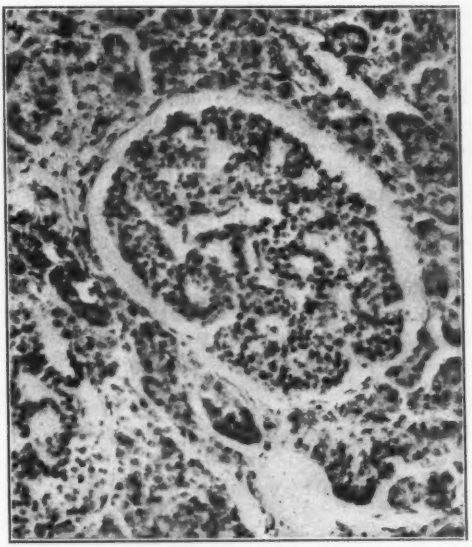

Fig. 2. Section showing hypertrophy of the Islands of Langerhans x 200.

It is unfortunate that no detailed clinical study of this case was possible; however, conditions beyond our control prevented it. The case is, therefore, presented without further comment as a case of glycosuria accompanied by the usual clinical symptoms of diabetes, in which the glycosuria disappeared and in which, at autopsy, fibrosis of the thyroid was found accompanying which there was partial fibrosis of the glandular elements of the pancreas associated with hypertrophy of the islands of Langerhans. We have seen (3) an almost as extensive fibrosis

of the thyroid associated with a case of Addison's disease in which both adrenal glands were completely destroyed by tuberculosis; and nearly as great an hypertrophy of the islands of Langerhans in another case (carcinoma of the head of the pancreas). In the later case, as in the one here recorded, the hypertrophy was chiefly in the body of the pancreas. In neither of these two cases was there any sugar in the urine. With these additional cases in mind we would be reluctant to decide whether in our own case the glycosuria was initiated by thyroid overactivity and receded after pancreatic fibrosis or whether the reverse occurred.

BIBLIOGRAPHY

1. Rohdenburg : Endocrinol. (Los Angeles), 1920, **4**, 63.
2. Friedman and Gattesman: Proc. Soc. Exper. Biol. & Med. (N. Y.), 1921, **18**, 281, and a later number not yet issued.
3. These cases were seen through the courtesy of Dr. L. Knox at St. Luke's Hospital, New York, to whom I am indebted for the privilege of reporting them here.

Book Reviews

INNERE SEKRETION. IHRE PHYSIOLOGISCHE GRUNDLAGEN UND IHRE BEDEUTUNG FÜR DIE PATHOLOGIE. Prof. Dr. Artur Biedl. 4 ed. Berlin & Vienna, 1922. Urban and Schwarzenberg. Band I, 1 Teil, 338 p.; Band III, 480 p., 8°.

The readers of this Journal will be very glad to know that a new edition of Biedl's well known monograph is now coming from the press. No endocrinologist needs a detailed introduction to a work which has so long been our standard authority.

Part 1 of Volume I includes a general introduction in which appears a particularly welcome fifty-page discussion of "constitutional" biology, a topic upon which there has been much loose writing. Several instructive diagrams are used to bring out the proportional bodily differences at various ages in both sexes. The factors determining "constitution" are carefully considered. The next fifty-six pages are given to methodology. The last two hundred pages are devoted to the thyroid and parathyroid glands.

Volume III is made up entirely of bibliography. Some citations as late as 1921 are found. It is gratifying to note that, as in previous editions, the original captions of the articles cited are included. Endocrinologists are much indebted to Prof. Biedl for the vast amount of irksome labor that the compilation of this volume has entailed.—R. G. H.

THYMUS UND BASEDOW, EIN BEITRAG ZUR FRAGE DER BEZIEHUNGEN BEIDER ORGANE. Dr. Erich Junge. Berlin, 1921. Verlag von Emil Ebering. 18 p.

The text of this brochure is as confused as its title. Some data are adduced as to whether the thymus should be removed in Graves' disease. A few pages are also devoted to "Thymustod." The author speaks of vagotonia as though the theories of Eppinger and Hess were established facts. More details are unnecessary.—J. K.

THE PITUITARY. Prof. W. Blair Bell. London, 1919. Balliere, Tindall & Cox. 347 p.

This book is an excellent, well illustrated monograph on the physiology, anatomy, pathology and pharmacology of the hypo-

physis. Every important question is thoroughly discussed with a good review of the literature and the author's own opinion is often given at the end.

For the most part, the literature is reviewed only through 1913 or 1914. The clinical part of the book is not always satisfactory; diabetes insipidus, Fröhlich's disease, etc., are simply described as being caused by a disease of the pituitary, while even in 1897, Loeb firmly denied this and considered that these are diseases of the midbrain. It is not mentioned that at least 40 per cent of acromegalics are also afflicted with a strange form of diabetes mellitus. The book has been read with much interest, and it is warmly recommended.—J. K.

PRACTICAL CHEMICAL ANALYSIS OF BLOOD. Victor C. Myers. St. Louis, 1921. C. V. Mosby Co. 121 p., 8°.

In the endocrinopathies practical blood chemistry is becoming of increasing importance. In Myers' book will be found a terse and readable presentation of the data needed in making determinations of blood constituents in studies of blood sugar curves, blood urea, etc. It will be found especially useful in the more careful studies in diabetes.—R. G. H.

Abstract Department

A case of ACROMEGALY. Faber (K.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 1400-1403.

A typical case of acromegaly. Examination in August, 1911, showed a total hemianopsia and diminishing of the other part of the visual field. Renewed examination in September, 1911, showed the visual field enlarged in both eyes and the left hemianopsia complete for red, but not for white. In 1919 the left visual field was normal. X-ray treatment was followed by considerable improvement.

—K. H. K.

A case of ACROMEGALY (Een geval von acromegalie). Tempelmans Plat, Maandbl. v. Specialische Geneesk. (Amst.), 1922, **5**, 8.

Demonstration of a case. No details are described.—J. K.

Examination of a boy with ADIPOSITY. Begtrup (E.), Ugesk. f. Læger (Copenhagen), 1921, **83**, 923-929.

In a boy, aged 11 years, with very marked adiposity there was found normal total metabolism. This was diminished by a stringent four months' limitation of diet. At the same time the protein and fat of the food were better utilized. It was very easy to obtain N-balance, even with low protein and low calorie diet. No endocrine disturbances could be recognized.—K. H. K.

Clinical ADRENAL insufficiency (Études cliniques sur l'insuffisance surrénales). Babonneix (L.), Monde Méd. (Par.), 1917, **26**, 225-229.

Reference verified from Index Medicus.

The pathogenesis of Addison's disease. Destruction of the ADRENAL medulla by a metastatic lymphangio-endothelioma of the peritoneum (Zur Pathogenese des Morbus Addisonii. Zerstörung des Nebennierenmarkes und des Grenzstranges durch ein Lymphangioendothelioma peritonei metastaticum). Bannwart (A.), Frankfurt. Ztschr. f. Path. (Wiesb.), 1921, **26**, 307-316.

The author refers to some cases of Addison's disease reported recently by Fahr and Reiche (Frankfurt. Ztschr. f. Path., 1920, **22**, 231-253), which supported the view that the suprarenal cortex was the primary seat of the disturbance causing Addison's disease. He reports the case of a male white subject, aged 45 years, from Hedinger's Laboratory at Basel. The patient was under observation approximately two years and died with a clinical diagnosis of Addison's

disease and malignant tumor of the peritoneum. The autopsy showed lymphangio-endothelioma of the peritoneum with metastases into the skin; subcutaneous fatty tissue; bone marrow; cervical mediastinum; bronchial, retroperitoneal and mesenteric lymph glands; lungs; pleura; **thyroid**; spleen; liver; intestine; both suprarenals; and both **testes**. The **thymus** was not made out. The spleen was slightly enlarged. The left adrenal was markedly enlarged with consistency increased; the cortex was approximately 3 mm. in thickness and poor in lipoid. Demarcation between the medulla and cortex was not made out. The right suprarenal was slightly larger than left, measuring 6x7x1.5 cm. Microscopic examination showed that the medulla of both suprarenals had been completely destroyed by tumor metastases while the cortex was well preserved. Bannwart thinks the case demonstrates with great clearness that typical Addison's disease may develop from isolated disease of the suprarenal medulla, thus supporting Wiesel and Hedinger in their contention that the malady is primarily a disease of the chromophil system.—D. M.

(ADRENIN) Remarks on caffein glycosuria (Remarques sur la glycosurie caféinique). Bardier (E.), Duchein (P.) & Stillmunkès (A.), Compt. rend Soc de biol. (Paris), 1922, **86**, 4-6.

Of endocrine interest in that the antagonistic action of **adrenalin** and caffein on the peripheral termination of sympathetic nerves is discussed.—T. C. B.

The effects of ADRENAL feeding upon the iodin content of the THYROID gland. Black (E. M.), Hupper (M.) & Rogers (J.), Am. J. Physiol. (Balt.), 1922, **59**, 222-226.

Dogs were fed on a standard diet to which was added either "adrenal residue," or adrenal nucleoprotein, or adrenalin crystals (P. D. & Co.). The controls were fed the standard diet only. One lobe of the thyroid was removed before beginning the experiment, and its iodin content determined by the Kendall method. After forty-five days of feeding the second lobe was removed and its iodin content determined. Adrenal residue can produce in the dog's thyroid a gain in iodin of an average of seventy per cent in forty-five days. Adrenal nucleoprotein causes a gain in iodin of fifty per cent. Adrenal crystals produce little if any gain. The extract of the entire gland, containing something more than pure adrenalin, therefore, has a direct effect upon the thyroid.—T. C. B.

Calorigenic effect of ADRENALIN in dogs. Boothby (W. M.) & Sandiford (I.), Am. J. Physiol. (Balt.), 1922, **59**, 463-464.

Subcutaneous injection of 0.5 mgm. adrenalin in man causes an increase in the rate of heat production. The rate of absorption of adrenalin approximates 0.0016 mgm. per kilo per minute. When

injected at this rate in dogs there is just a perceptible calorigenic effect. Intravenous injections of 0.0045 mgm. per kilo per minute produces a definite calorigenic effect of from 10 to 40 per cent. These figures are comparable with those obtained by Stewart and Rogoff and by Cannon under normal conditions, and lead to the conclusion that the adrenals can spontaneously discharge sufficient adrenalin to effect the rate of heat production, possibly by chemical stimulation of cellular activity.—T. C. B.

(ADRENAL) Pathogenesis of gastric ulcers (Contributo sperimentale alla patogenesi dell'ulcera gastrica). Brisotto (P.), Riforma med. (Napoli), 1922, **38**, 127-129.

Brisotto reports a case of a dog, which, after removal of an adrenal, showed asthenia, gastric disturbances with vomiting, and at autopsy a pyloric ulcer involving the muscularis and mucosa. Similar results were obtained through operations on the vagus and on the celiac plexus, though the ulcer was not always found.—G. V.

SUPRARENAL insufficiency and organotherapy. Cohoe (B. A.), Penn. M. J. (Harrisburg), 1922, **25**, 345-346.

A brief résumé of the acute, subacute and chronic types supposedly dependent upon suprarenal insufficiency; acute rapidly fatal cases are thought to be due to hemorrhage into the suprarenals; Addison's disease is referred to; the chronic functional type with asthenia, lethargy, circulatory weakness, cold hands and feet is mentioned. The author is conservative in his statements concerning organotherapy with suprarenal extracts, seeming to agree with those who report little or no benefit from their use. He distinguishes between the drug effect of epinephrin, as used prophylactically in anaphylactic shock or to abort attacks of asthma, and any supplementary rôle in so-called states of suprarenal insufficiency. There is no certain evidence that suprarenal extract given by mouth has any curative power.—H. L.

(ADRENAL) Therapeutic value of "adrenofer" (Richereche sul valore terapeutico dell'adrenofer). Connio (A.) & Crosa (A.), Gazz. med. sicil. (Catania), 1917, **19**, 344-346.

Reference verified from Index Medicus.

Blood pressure and pulse reactions to ADRENIN in sick children (Modificazioni della pressione e del polso per effetto dell'adrenalina in bambini ammalati). De Angelis (F.), Pediatria (Napoli), 1921, **29**, 542-547.

The effect of adrenalin on sick children as regards the kind of reaction provoked by the individual pathological condition and the possibility of a special reaction in special groups or types of disease has been studied. The author found that the injection of adrenalin

(1 cc., 1:1000) causes in sick children a rapid rise of the pressure, manifest after the first 10 minutes, reaching its maximum within 30 minutes, to slowly decrease in from 2½ to 3½ hours. Both maximum and minimum, but especially the maximum pressures were studied. Children with cardiac or cardio-vascular disorders showed a reaction less marked and of shorter duration than normal. The pulse showed initial acceleration, followed immediately by retardation, but maintaining strong systolic tension.—G. V.

Complementing activity of the blood serum with relation to ADRENAL insufficiency. Ecker (E. E.) & Rogoff (J. M.), J. Immunol. (Balt. & Cambridge, Eng.), 1921, **6**, 355-361.

The rabbit was used in these experiments because of the fact that a fair proportion of these animals survive complete bilateral adrenal ablation. Accessory adrenal tissue is sometimes present in the rabbit; it always consists of cortical substance and not medulla. At autopsy upon the six rabbits used only one was found to still possess a small mass of adrenal tissue near the liver. An antisheep hemolytic system was employed, the complement being supplied in quantities of 0.025 to 0.2 cc. of the serum of the epinephrectomized rabbits. The authors conclude that the complementing power of the blood serum of rabbits is not modified by unilateral or bilateral adrenal extirpation.—J. P. S.

Raynaud's syndrome in ADRENAL disease. Faber (K.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 2112-2114.

A woman, aged 47 years, showed typical symptoms of Raynaud's disease; cyanosis, coldness of the fingers, panaris, and later on, gangrene of one finger. She suffered with edema of the legs and sometimes of the face. After a month, the patient became nauseated. There was further pigmentation of the skin, albuminuria and, lastly, convulsions and death. Autopsy showed the left adrenal gland normal; the right adrenal gland was destroyed by tuberculosis; the kidneys showed nephritic changes. The **thyroid, hypophysis** and **thymus** were normal.—K. H. K.

The pigments of the ADRENALS. Findlay (G. M.), J. Path. & Bacteriol. (Cambridge), 1919, **23**, 482-489.

There is a striking similarity between the distribution of the vegetable lipochromes and one of the accessory food factors, fat soluble A. The author studied the content of fowl and human adrenals in lipochrome and melanin. The amount of lipochrome in the adrenals of hens can be varied by alterations in the lipochrome content of the food. He found, in addition to carotin and xanthophyll, a possible third substance in the hen's adrenals that seems to be related to the lipochromes. In acute pathological conditions in human beings, e. g., in acute infections such as pneumonia and

meningitis, the amount of lipochrome pigment in the adrenals is moderately increased. No melanin pigment was found. In chronic affections, such as carcinoma, tuberculosis and diabetes, the lipochromes showed a considerable increase and there was almost always some melanin present both in the cortical and in the medullary cells. Since lipochrome pigment is of exogenous origin, its presence in the adrenals must be looked upon as a true infiltration, analogous to fatty infiltration and occurring in conditions involving a decrease in the activity of the cell. Melanin pigment, on the other hand, appears to be entirely endogenous in its origin, and to be formed in conditions of long-continued depression of the cell. Such depression may arise physiologically in infancy and old age, and in almost all chronic pathological conditions, more particularly in tuberculosis and cancer.—J. P. S.

The diaphoretic action of ADRENIN (Ueber die bei iontophoretischer Einführung von Substanzen zu beobachtenden Hautreaktion). Freund (E.), Ztschr. f. phys. u. diätet. Therap (Leipz.), 1921, **25**, 145-160.

Adrenalin acts as a stimulant to the local secretion of sweat in man. In the reaction the local application of heat plays a significant rôle. The antagonistic action of adrenalin and pilocarpin can be seen in the vasomotor apparatus of the skin.—F. S. H.

(ADRENIN) The secretion of sweat, Part 1. Supposed inhibitory nerve fibers on the posterior nerve roots. Secretion after denervation. Langley (J. N.), J. Physiol. (Lond.), 1922, **56**, 110-119.

Of endocrine interest in that it is shown that adrenalin only causes secretion of sweat by virtue of the fluid in which it is dissolved, Ringer's solution injected into the pad of a cat's foot commonly causing more secretion of sweat than does adrenalin.—T. C. B.

ADRENAL function. III. Variations in the vasomotor action of the great splanchnic nerve in various species of animals. Gley (E.) & Quinquaud (A.), J. de physiol. et de path. gén. (Par.), 1921, **17**, 355-364.

Observations on dogs, cats, rabbits, and a fox show that the form of reaction following splanchnic excitation differs in different species of animals. This fact does not lend support to the theory that the reaction depends in part on the adrenal secretion.

—Chem. Abst., **16**, 754.

Pathological ADRENAL alterations in domestic animals (Le alterazione delle capsule surrenali in rapporti di diversi stati patologici degli animali domestici). Grimaldi (E.), Clin. vet. (Milano), 1917, **39**, 671-700.

Reference verified from Index Medicus.

Epilepsy and hyperfunction of the ADRENALS (Krampfkrankheiten als Hyperfunktion der Nebenniere). Hanke, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 119.

The author removed an adrenal in two cases of epilepsy. In one case there was a slight temporary result; in the other, no result whatever was seen.—J. K.

The relation of the ADRENALS to fatigue. Hartman (F. A.), Am. J. Physiol. (Balt.), 1922, **59**, 463.

The denervated pupil (superior cervical ganglion removed) of a normal cat usually dilates after working in a treadmill for a time. Dilatation increases as the work proceeds. Removal of both adrenals abolishes the "fatigue" dilatation. Cutting the splanchnic to a single remaining adrenal reduces or abolishes "fatigue" dilatation. Cats with but a single adrenal, and that denervated, cannot work so hard, nor travel so far, as normal animals. After regeneration of the nerve, the pupil reaction reappears, and the animal works better. Epinephrin increases the ability to do work and withstand fatigue.
—T. C. B.

Action on blood pressure of ADRENIN injected into the subarachnoid space. Kasahara (M.), Kyoto Igakkwai Zashi, **18**, No. 2; Abst., Jap. Med. World (Tokyo), 1921, **1**, 26.

Injection of commercial adrenalin into the subarachnoid space of the rabbit causes a lowering of blood pressure due to the acidity of the preparation. The work of Meltzer and Auer along this line has no clinical significance. An injection of 0.7% saline into the subarachnoid space without first removing cerebrospinal fluid causes a rise in pressure in both the cerebrospinal cavity and the blood vessels. This rise is slow and is maintained for a comparatively long period. Clinically subarachnoid injection of adrenalin has no more influence than 0.7% saline.—R. G. B.

ADRENAL toxic serum and atheroma. Marabotto (F.), Ann. d. Ist. Maragliano p. la cura d. tuberc., etc. (Genova), 1918, **8**, 209-224.

Reference verified from Index Medicus.

The influence of ADRENIN anemia on the progress of experimental tuberculous infection (L'influenza dell'anemia adrenalinica sul decorso della infezione tubercolare sperimentale). Maragliano (D.), Riforma med. (Napoli), 1921, **37**, 1082.

Adrenalin anemia renders more severe local alterations due to inoculation of tuberculous products. The invasion into the neighboring ganglia and the generalization of the process are not influenced.—G. V.

Influence of glands with internal secretions on the respiratory exchange. III. Effect of SUPRARENAL insufficiency (by removal) in thyroidectomized rabbits. Marine (D.) & Baumann (E. J.), Am. J. Physiol. (Balt.), 1922, **59**, 353-368.

In a previous paper it was shown that removing or crippling the suprarenals resulted in marked changes in the respiratory exchange, and possible causes of increased heat production were discussed. The present paper describes experiments undertaken to obtain data on the question whether the **thyroid** is an important factor in the increased heat production following suprarenal ablation. The procedure was to observe the normal heat production in six rabbits for two weeks, then completely remove the thyroids and measure heat production, then remove the suprarenals and again observe the heat production until the animals died or were sacrificed. Protocols in full are given, with a discussion of the results. The conclusion is that removal of the thyroid prevents or greatly lessens the increased heat production caused by partial destruction of the suprarenal cortex. While epinephrin in large doses may stimulate the thyroid, the insufficiency of the regulatory, inhibitory and restraining effects of the cortical influence is much more important in thyroid activity and tissue oxidations in rabbits. Glandular interrelations such as the **gonads** may be involved (See also Am. J. Physiol., 1922, **59**, 439-440).—T. C. B.

The influence of ADRENALIN on metabolism in isolated skeletal muscle. Martin (E. G.) & Armitstead (R. B.), Am. J. Physiol. (Balt.), 1922, **59**, 37-43.

Boothby and Sandiford report a "specific dynamic action of adrenalin chloride on all the cells of the body causing them to metabolize more rapidly under its influence." Metabolism proceeds in isolated muscle with the production of heat and carbon dioxide, and it is this metabolism that is investigated. The method proposed by Haas was modified to suit the special requirements. The sartorius muscles of the frog were carefully excised, weighed, and suspended in neutral Ringer's solution to which had been added eight drops of 0.02 per cent phenolsulphonephthalein solution. All gaseous exchange with the outside air was guarded against. When the color of the solution had definitely changed (about 20 minutes) the muscles were removed, the pH of the solution again determined, and the production of H ions per gram of muscle computed. By this means it was determined that the excised sartorius during the first half hour after excision averages a pH production of 110×10^{-8} at 20 degrees C. The addition of adrenalin to the solution augments this resting metabolism from 25 to 400 per cent, according to the concentration of the adrenalin. This is interpreted as confirming the view of Boothby and Sandiford.—T. C. B.

(ADRENAL) Addison's disease (Morbo di Addison). Molinari (G.), Riforma med. (Napoli), 1921, **37**, 1024-1026.

The article is a thorough discussion of Addison's disease as regards the most recent conceptions of its etiology and nature. The author insists on a primary adrenal as well as sympathetic etiology He values highly wholè adrenal gland treatment and favors the use of adrenalin only in emergency cases.—G. V.

ADRENAL hematomas (Contributo allo studio degli ematomi delle capsule surrenale). Moramarco (G.), Riv. osp. (Roma), 1916, **6**, 1-17.

Reference verified from Index Medicus.

The influence of ADRENIN on blood sugar (Uber die Wirkung des Adrenalins auf den Blutzucker). Petenyi (G.) & Lax (H.), Biochem. Ztschr. (Berl.), 1921, **125**, 272-282.

These observations were made in the First Medical Clinic of the University of Budapest. The authors determined the influence of subcutaneous injections of epinephrin in four adults, two children about the age of puberty, and four nursing infants. The dosages used were 1.0 mg., 0.6 mg. and 0.1 to 0.3 mg. epinephrin, respectively, for the three age groups. The **blood sugar** was determined by the Bang procedure one, two, three, four, six and eight hours after the injections. Invariably they observed hyperglycemia followed by hypoglycemia as has been reported by many others. In addition to the above mentioned normal subjects, they studied the effect of epinephrin injection in sixteen nursing infants suffering from infantile tetany. In these cases hyperglycemia following epinephrin injection was less marked than in normal individuals and did not always occur, while hypoglycemia always followed, just as in normal persons, and was even more pronounced in degree and duration.—(D. M.) E. J. B.

(ADRENIN) Urine formation in the perfused kidney. The influence of alterations in renal blood pressure on the amount and composition of urine. Richards (A. N.) & Plant (O. H.), Am. J. Physiol. (Balt.), 1922, **59**, 144-183.

It was found that increased urine flow follows administration of adrenalin as well as splanchnic stimulation.—T. C. B.

Urine formation in the perfused kidney. The influence of ADRENALIN on the volume of the perfused kidney. Richards (A. N.) & Plant (O. H.), Am. J. Physiol. (Balt.), 1922, **59**, 184-190.

"When the kidney of the dog or rabbit was excised and perfused with hirudinized blood at a constant rate of flow, the addition

of a small amount of adrenalin to the blood caused rise in perfusion pressure and swelling of the kidney. This result is interpreted as evidence that the vas efferens is constricted by adrenalin with consequent rise of intraglomerular pressure and distention of the Malpighian bodies. It is regarded as explanatory of the diuresis caused by adrenalin, splanchnic stimulation and medullary stimulation."
—T. C. B.

The action of minute doses of ADRENALIN and PITUITRIN on the kidney. Richards (A. N.) & Plant (O. H.), Am. J. Physiol. (Balt.), 1922, **59**, 191-202.

If adrenalin causes a rise of perfusion pressure, increased volume of the kidney and diuresis in the perfused kidney, it is believed that similar conditions might be demonstrated in the intact animal. The essential difference would be that in the perfused kidney the blood is driven at a constant rate through the kidney regardless of the state of constriction of the blood vessels; while in the intact animal the renal blood flow would be diminished by vasoconstriction. In attempting to solve this problem rabbits, cats and dogs were used. The rabbits were made diuretic before the operation by feeding carrots; the dogs by injecting glucose solution into the stomach some hours before the experiment. Carotid pressure was recorded. Injections were into the jugular vein, and were not "washed in." Some animals were completely eviscerated after ligating all the coeliac and mesenteric arteries and the portal vein; in other the coeliac axis was not ligated, and only the jejunum, ileum and large intestines removed. The vagi and splanchnic were cut. Both suprarenal veins were ligated and the right kidney was ligated in some, excised in others. After ligature of the abdominal aorta below the origin of the left renal artery, the inferior vena cava was prepared for the Barcroft-Brodie method of estimating blood flow through the kidney. The volume of the left kidney was recorded by an oncometer and the urine flow by the drop method from a cannula in the left ureter. "Under the influence of minute doses of adrenalin and pituitrin, blood flow through the kidney may be decreased, while the kidney volume and urine elimination may be increased. Considerations are presented in support of the belief that this combination of events reveals a slight degree of constriction of the efferent vessels, with consequent increase in glomerular pressure. The experiments are interpreted as bearing upon the problem of glomerular regulation of urine formation."—T. C. B.

On the ADRENALIN content of the suprarenal capsules, determined by chemical methods and by physiological methods (Sur la teneur en adrénaline des capsules surrénales, déterminée par la méthode chimique et par la méthode physiologique). Richaud (A.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 26-28

A comparison of the effects of pure l-adrenalin with solutions of the dried and powdered suprarenals of commerce, using the blood pressure curve as an index of their potency, after the method of Cushny. The curve furnished by 0.00002 gm. adrenalin is duplicated by 0.0025 gm. dried capsule, which corresponds to 0.0000066 gm. of adrenalin calculated from the chemical titer. Either there are other pressor substance in the capsule, or the process of extraction does not furnish the total quantity of adrenalin present. The latter is most probable.—T. C. B.

Cheyne-Stokes respiration, Part 1. Production by ADRENALIN. Roberts (F.), J. Physiol. (Lond.), 1922, **56**, 101-109.

In a previous paper (J Physiol., 1921, **55**, 346) the author mentions that rabbits and cats exhibit Cheyne-Stokes respiration after the intravenous injection of a large dose of adrenalin. The present paper describes the character of the respiration, and explains the cause. If a certain blood pressure is necessary to provoke respiration it may be that Cheyne-Stokes respiration has a vascular origin. To test this, rabbits were used. The blood pressure can be taken in the circle of Willis simultaneously with the carotid pressure by introducing a cannula into the common carotid close to the bifurcation into internal and external, the latter being tied off. The pressure in the circle of Willis rises and falls with that in the carotid, and is surprisingly high, being very little less than in the aorta. It may reach 160 mm. or more after the injection of adrenalin. The number of experiments is not given, but the tracings show that as the pressure reaches the maximum after the injection of adrenalin apnea comes on, to give place to a resumption of respiration as the pressure falls. This is continued rhythmically. The conclusion is that the Cheyne-Stokes respiration sometimes produced by the injection of adrenalin is of two kinds: major waves with a periodicity of 30 to 80 seconds, and minor waves with a periodicity of 5 to 15 seconds. The first are due to rhythmic changes in the caliber of the cerebral vessels; the second seem to be associated with oscillations in general blood pressure.—T. C. B.

Experimental study of clinical application of ADRENALIN. Sorna (D.), Gun-i-dan Zasshi, No. 105; Abst., Jap. Med. World (Tokyo), 1921, **1**, 23.

The adrenalin used was that of Sankyo and Co., Tokyo. It was assayed by the Meltzer-Ehrmann frog-eye method. For clinical administration adrenalin should be diluted with distilled water, 0.1% hydrochloric acid or 2.0% boric acid, and is best given by intravenous injection. When given hypodermically in a large quantity of physiological saline or sodium bicarbonate (1% solution) or through a steam inhaler its efficacy is greatly diminished.—R. G. B.

ADRENAL extirpation in epilepsy (Nebennierenexstirpation bei Epilepsie). Sultan (G.), Deutsche med. Wchnschr. (Berlin), 1922, **48**, 153-155.

In 5 cases of epilepsy an adrenal was removed. In 2 cases the blood pressure was somewhat raised after the operation; in a third, it was slightly lowered. Schlund has stated that after the operation lymphopoenia with neutrophilic leucocytosis is found. This is true, but it is seen also after simple ether narcosis. In one case the **blood sugar** was somewhat increased; in the four other cases the operation had no effect whatever. The effect of the operation on the epilepsy was almost absolutely negative.—J. K.

The action of ADRENIN on the surviving uterus (Umkehr der Adrenalin-wirkung auf den überlebenden Uterus durch Ionenverschiebung). Turolt (M.), Arch. f. gynaek. (Berl.), 1922, **115**, 600-610.

An excess of potassium or calcium salts in the nutrient solution in which the surviving uterus from either guinea-pig or man is suspended causes a change in stimulation of this tissue. While adrenalin inhibits the movements of the gravid and non-gravid uterus of the guinea-pig in normal Ringer's solution, when an excess of calcium is present, stimulation by adrenalin takes place in both cases. On the other hand, potassium salts which inhibit the rhythmic movements have no effect on the adrenalin action. On the human uterus, however, which adrenalin stimulates in either the gravid or non-gravid condition, an excess of calcium produces inhibition of automaticity, and potassium an augmentation. The inhibitory action of the calcium only hinders the adrenalin action on the non-gravid. These studies show that the two ions, calcium and potassium, have exactly the opposite effect from adrenalin on both uterus preparations.—F. S. H.

(ADRENAL) Addison's syndrome in incomplete Recklinghausen's disease (Sindrome addisoniana in una forma incompleta di malattia Recklinghausen). Vignolo-Lutati, Riforma med. (Napoli), 1917, **32**, 1061-1064.

Reference verified from Index Medicus.

Sudden death in atrophy of the ADRENAL cortex (Ueber plötzliche Todesfälle bei Atrophie des Nebennieren-markes). Zimmerman (R.), Monatschr. f. Geburtsh. u. Gynaek. (Berl.), 1922, **56**, 259-270.

Report of two cases as described in title. No marked pigmentation was present.—F. S. H.

Criteria in "CONSTITUTION" researches (Über Konstitutionsforschung in der normalen Anatomie. Einige Richtlinien). Hammar (J. A.), Anat. Anz. (Jena), 1916, **49**, 449-474.

DIABETES. Barlaro (P. M.), Prensa méd. argentina (Buenos Aires), 1916, ii, Suppl., 218-220.

Reference verified from Index Medicus.

DIABETE ed acidosi. Castellino (P.), Folia med. (Napoli), 1917, **745**, 694-817.

Reference verified from Index Medicus.

A method to determine acetone, diacetic acid, oxybutyric acid and dextrose quantitatively in DIABETIC urine. Claudius (M.), Hosp.-Tid. (Copenhagen), 1921, **64**, 97-108.

The author describes in detail a method to determine quantitatively the substances named. The principle is oxydizing with sodium iodide and sulfuric acid. The precipitated iodide is absorbed by tetrachlormethane and titrated with thiosulfate.—K. H. K.

Treatment of DIABETES in common practice. Hagedorn (H. C.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 1939-1945.

The author describes the theoretical foundation for the American treatment of diabetes (Allen and Joslin). He further describes the manner in which the practitioner can best carry out this treatment.—K. H. K.

The duration of fatal attacks of DIABETES mellitus. Heiberg (K. A.), Hosp.-Tid. (Copenhagen), 1919, **62**, 1137-1140.

Examinations of reports of fatal diabetes during a period of 10 years in Danish towns (820 men and 683 women) shows that the duration of the disease is much longer in old age than in youth and much longer for men than for women. However, the apparent longer duration in men may be due to the fact that men have their urine examined for life insurance oftener than do women.—K. H. K.

(DIABETES) Case of glycosuria of combined nature. Holst (J. E.), Ugesk. f. Læger (Copenhagen), 1921, **83**, 1072-1081.

The author reports the case of a man, aged 47 years, with glucosuria, which shows a transition form between true diabetes and the so-called renal diabetes. The result of the **blood-sugar** examinations (fasting and eating sugar on bread) is illustrated by a curve. The case shows continued glucosuria with very low blood-sugar, absence of diabetic symptoms, no progression for 23 years (without treatment), but blood-sugar curves corresponding to those which are found in true diabetes.—K. H. K.

The problems of modern DIABETIC treatment. Janney (N. W.), Northwest Med (Seattle), 1922, **21**, 47-49.

An analysis of the most recent 100 cases of diabetes observed by Janney, shows that 87 per cent had received previous medical treatment. Of this number 79 per cent had merely received qualitative restrictions of diet, but only 21 per cent accurately weighed diets. The author, with this experience as a text, criticizes the methods of the average general practitioner and even general internist, and insists that very few of them are equipped to manage this disease properly, with the result that the mortality is considerably higher than it should be. Some blame also attaches to the patient who refuses to follow directions, even though attractive menus are offered him. "In all but the very lightest cases a strict quantitative diet must be enforced over a long period; in all severe cases, for the duration of the patient's life." The exacting necessities of modern diabetic treatment demand a diabetic laboratory, an adequate clinical chemical laboratory, professional judgment, skill and experience. All new hospitals should include a metabolic pavilion with commodious diet kitchen, chemical and respiratory metabolic laboratory, sick rooms, a diabetic class and an out-patient department with instruction of the poor in diabetic cookery.—H. L.

The use of raw starch in the treatment of DIABETES. Knerr (E. B.), J. Missouri M. Ass. (St. Louis), 1916, **13,** 442-445.

Reference verified from Index Medicus.

Negligible GLYCOSURIA. Leyton (O.), Practitioner (Lond.), 1922, **108,** 113-118.

The author introduces the term "negligible glycosuria" in preference to "diabetes innocens" "renal glycosuria" and "glycosuria without hyperglycemia." He refers to that group of people who excrete about 0.5 per cent dextrose in their urine, but have no other manifestation of diabetes mellitus. He prefers the term "negligible glycosuria" because the cause of the condition is not known. These cases are not early diabetes mellitus. Neither the quality nor quantity of food consumed makes any appreciable difference to the percentage of sugar in the urine excreted. These cases should not be confused with true diabetes mellitus. They do not require any treatment. Leyton has examined 18 such individuals in the past two years. He noted a familial tendency. Seven cases are mentioned that have histories of glycosuria averaging 18 years and none has developed symptoms or signs of diabetes mellitus.—H. L.

Influence of lumbar puncture on the polyuria and glycosuria of DIABETES mellitus (Influence frènatrice de la ponction lombaire sur la polyurie et la glycosurie du diabète sucré). Lhermitte (J.) & Fumet (C.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46,** 322-328.

Lumbar puncture in 2 cases of diabetes mellitus brought about a diminution in urinary secretion and sugar elimination. This may indicate a central origin for the disease.—F. S. H.

Emotional DIABETES in forensic medicine (Il diabete mellito da emozione in medicina legale). Maganami (R.), Arch. di antrop. crim. [etc.] (Torino), 1916, **37**, 181-194.

Reference verified from Index Medicus.

Sparing action exercised by the fats against the destruction of protein in DIABETICS in a state of nitrogen denutrition (Action d'épargne exercée par les graisses vis-a-vis de la destruction d'albumine chez les diabétiques en état de dénutrition azotée). Maignon (F.), Compt. rend Soc. de biol. (Par.), 1922, **86**, 111-114.

Deals with the sparing action of fats and a treatment of diabetes based upon it.—T. C. B.

Mastoid operation in DIABETES. Mygind (H.), Hosp.-Tid. (Copenhagen), 1921, **64**, Oto-laryngeal Soc. Reports, 108-111.

Since 1905 the author has treated 1500 patients with acute suppuration of the middle ear. Only 6 of these were complicated with diabetes; 5 of them were operated upon. Four died in coma within a few days after the operation. The complication of diabetes with otitis media is rather rare, but the prognosis is bad. Perhaps the coma is produced by a shock effect.—K. H. K.

DIABETES in the son of a syphilitic (Diabète avec aréflexie chez un fils de syphilitique). Pinard (M.) & Mendelsohn (E.), Bull. et mem. Soc. med. d. hôp. de Par., 1922, **46**, 397-404.

Antiluetic treatment of this case resulted in disappearance of sugar from the urine.—F. S. H.

Hypophysis extract in DIABETES mellitus (Sulla efficacia degli estratti ipofisari nella cura del diabete mellito). Vigevani (G.), Osp. maggiore (Milano), 1917, **4**, 530-533.

Reference verified from Index Medicus.

The therapeutic action of pituitrin in DIABETES INSIPIDUS (Sur l'action thérapeutique de la pituitrine dans le diabète insipide). Démètre (P. E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 308-314.

In diabetes insipidus a renal element is present which is associated with a permanent deficiency of pituitary secretion. This secretion has a direct action on renal as on all other epithelium. The influence of the hypophyseal secretion is sufficient to explain the mechanism of the polyuria in diabetes insipidus. Pituitrin exerts a direct and transitory effect on the polyuria.—F. S. H.

Infundibular polyuria. Syphilitic DIABETES INSIPIDUS (La polyurie infundibulaire. La diabete insipide syphilitique). Lhermitte (J.), Ann. de méd. (Par.), 1922, **11**, 89-127.

A review and discussion of the origin of diabetes insipidus together with the presentation of certain histological studies of infundibular-tuberal lesions of syphilitic nature. These studies showed that the lesions were limited exactly to the infundibulum and the tuber cinereum. The lesions were meningeal, vascular and neural. That the processes were syphilitic inflammations was undoubted. These facts contribute considerable doubt as to the soundness of the idea that the polyuria of diabetes insipidus takes its origin directly, if at all, in the **hypophysis**.—F. S. H.

(ENDOCRINE ORGANS) Further studies on substances with specific action prepared from single organs. VI. (Weitere Untersuchungen über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. VI.) Adberhalden (E.) & Gellhorn (E.), Arch. f. d. ges. Physiol (Berlin), 1922, **193**, 47-83.

(See Endocrinology, **5**, 643.) The **testis** optones obtained by hydrolysis with 10 per cent sulphuric acid excite the automaticity of quiescent frog heart-strips, while the hydrolysate produced by enzyme and autolytic action has no such effect. Subsequent hydrolysis of the latter with 10 per cent sulphuric acid gives a product with the characteristic action. This is strengthened by removal of substances soluble in alcohol. Enzyme-produced **placenta** optones increase the contractions of Straub's preparations after pulse diminution, while acid-produced optones from placenta produce only a negative inotropic action (and a negative chronotropic action on heart-strips). **Thyroid** and **struma** hydrolysates excite the automaticity and tonus of surviving frog esophagus. In the same concentration placenta optones (acid or enzyme produced) are markedly paralyzing; the acid optone in weaker concentration increases the contractions. **Thyroid, pituitary, thymus, ovary, placenta** (enzyme) and **testis** (acid) optones exercise a more or less strong capillary dilating and sometimes artery dilating effect, and inhibit or lessen the action of adrenalin. It is suggested that these "incretions" play a significant rôle as regulators of the capillary mechanism.—A. T. C.

Uricolytic power of the ENDOCRINE glands (Sul potere uricolitico delle ghiandole e secrezione interna). d'Amato (L.) & de Nunno (R.), Pathologica (Genova), 1917, **9**, 205-210.

Reference verified from Index Medicus.

PLURIGLANDULAR insufficiency. Askgaard (V.), Hosp.-Tid. (Copenhagen), 1921, **64**, Neurol. Soc. Reports, 19-20.

A girl, aged 10 years, since her fifth year had complained of headache and dullness. She had always been very fat. The

following symptoms were manifested: convergent strabismus, adiposity, and shortness of arms and fingers. X-ray examination showed irregularity of the epiphyseal lines as in achondroplasia. —K. H. K.

(INTERNAL SECRETION) Multiple calcification of the muscolotendinous sheets (Sopra un caso di calcificazione multipla delle guaine muscolo-tendinee). Cantelmo, Riforma med. (Napoli), 1921, **37**, 1083.

The disorder in a subject, 25 years old, began with tumefactions, which, in a few months, opened, discharging a kind of calcareous paste formed of calcium carbonate and phosphate. Both legs were affected; the process began with the vessels, their walls being thickened and lumen reduced. There was also found atrophy of the muscles, protruding **thyroid**, sexual frigidity and asthenia. The case is thought to be due to endocrine dysfunction.—G. V.

ENDOCRINE deformity (Dismorfe endocrine). Giannuli (F.), Riv. di antrop. (Roma), 1919, **21**, 215-234.

Reference verified from Index Medicus.

Experimental studies on INTERNAL SECRETION. Harada (S.), Tokio Igakkwai Zasshi; Jap. Med. World (Tokyo), 1921, **1**, 17-18.

The author fed desiccated glands of internal secretion of cattle to tadpoles and young fish. Controls were fed with liver. Tadpole growth and metamorphosis was as follows: Normally the right fore leg first began to develop, then both legs developed simultaneously, while the left leg developed first least frequently. When fed with **thyroid** extract the frontal walls of the respiratory tube and margins of the tail fin disappeared first, then the left fore limb usually developed. This might have been due to an abnormally augmented metabolism caused by the thyroid hormone. These animals were found to have smaller thyroid and a smaller **pituitary** body, while the **testes** were larger than in the controls. The range of stimulation by galvanotropism was greatly lowered, possibly due to hormonic control. This change took place within a few hours and returned to normal in 3-4 days. Iodothyrin as well as iodonal had nearly the same effect as thyroid. Lipoiodin and iodostarin produced no abnormal metamorphosis. In **thymus** fed tadpoles metamorphosis was slightly retarded. If the thymus was mixed with wheat flour there was an irregular course of development. Thymus feeding had no marked effect on the range of galvanotropism. Pituitary feeding caused an increase in the length of the body. The relative increase in length was more marked when the posterior lobe alone was used. Those fed with anterior lobe had a slightly large **ovary**, but a small pituitary and a small thyroid. Adrenal cortex feeding caused poor growth. The **pancreas** and the thyroid seemed

somewhat smaller. Those fed with ovary had larger ovaries than the controls. The effect on body growth was not mentioned. The metamorphosis of the goldfish, Oryzias latipes and the carp have been similarly affected.—R. G. B.

Osteopsathyrosis and ENDOCRINE glands (Osteopsatirosi e ghiandole endocrine). Giorgi (E.), Riforma med. (Napoli), 1921, **37**, 787.

The post-mortem examination of a ten months' infant revealed a definite condition of fragilitas osseum with multiple fractures; there was found besides chronic hypophysitis, diffuse, irregular adrenal medulla and hyperplasia of the interstitial cells of the testis. There had been in life a 3 plus cutaneous tuberculin reaction. The initial cause is given as tuberculosis from a maternal focus, the determining endocrine dysfunction being a consequence of the infection.

—G. V.

INTERNAL SECRETION and autolysis (Autolisi e secreziones interne). Izar (G.) & Fagiuoli (A.), Sperimentale. Arch. di biol. (Firenze), 1916, **70**, 265-327.

Reference verified from Index Medicus.

Action of the INTERNAL SECRETIONS upon experimental cancer. Korentschewski & Kenow, Soc. Belga Biol., 1920, (May); abst., Pathologica (Genova), 1922, **13**, 60.

Castration in the dog facilitates the development of sarcoma; but it does not have any influence on the cancer of mice. **Thyroidectomy** seems to increase its development in dogs as well as in mice. Thyroid feeding retards the development, **thymus** feeding increases it. Mice fed with boiled tumor extract are less receptive than the controls.—G. V.

(ENDOCRINE GLANDS) Treatment of the métrorrhagias of young girls (Le traitement des métrorragies des jeunes filles). Hartmann (H.), Gynéc. et obst. (Paris), 1922, **5**, 81-83.

In a large majority of the transitory or prolonged changes in the menstrual flow there is an endocrine factor which has followed on from some infectious or chronic disease. Daily administration of 25 mg. **thyroid** extract; 0.20 gm. **pituitary** extract and 0.05 gm. **adrenal** extract is recommended.—F. S. H.

(ENDOCRINE GLANDS) Glandular dystrophies and particularly mono-symptomatic dystrophies (Dystrophies glandulaires et particulièrement dystrophies mono-symptomatiques). Hutinel (V.) & Maillet (M.), Ann. de méd. (Par.), 1921, **10**, 422-445.

A continuation of the review previously noted.—F. S. H.

INTERNAL SECRETION and the hormones. Krabbe (K. H.), Naturens Verden (Copenhagen), 1921, 1-8.

A short popular review of the functions of the different glands of internal secretion.—K. H. K.

Modifications in the ENDOCRINE glands and blood of chickens injected with adrenalin and cholin (Modificazioni nelle ghiandole endocrine e nel sangue di polli injettati con adrenalina e colina). Pighini (G.), Bioch. e Terap. Sperim. (Milano), 1921, **8**, 140-154.

Experiments with **adrenalin** (1% in dose of 1 cc.) were made on 15 chickens ranging in age from 2½ to 18 months. The older subjects stood the injections much better than the younger. Cholin injections (1% cholin hydrochlorate, Merck) of 0.5 to 1 cc. were made in 5 chickens from 2½ to 18 months of age. The organs examined besides the blood were the cerebrum, **hypophysis, thyroid, liver, spleen, pancreas, kidneys, testes, ovaries, thymus** and **adrenals.** The thymus, adrenals, spleen and blood showed much more accentuated histological changes than the others. The thyroid showed modifications with cholin injections. The other organs reacted only in case of acute intoxication, as in any toxic condition. In hyperadrenalized animals there was found parenchymatous degeneration of the thymus, shown by extreme diminution of the lymphatic elements of the cortex, the reduction of Hassall's corpuscles, and lipoid degeneration of the epithelial elements. The Malpighian lymphoids of the spleen were greatly reduced; there was hypertrophy of the chromaffin tissue of the adrenals, with diminution of the lipoids of the cortex. There was neutrophil leukocytosis (pseudoeosinophilia) in the blood. Animals treated with cholin showed hyperfunction of the thymus with hypertrophy of the medulla, conspicuous increase of the Hassall's corpuscles, many forms of hypertrophy of the epithelioid cells (giant, myoid cells), colloidal cysts, and thyroid with Basedowian characteristics. In the spleen was hypertrophy of the Malpighian corpuscles. A tendency to hypertrophy of the cortex was found in the adrenals. There was slight polynucleocytosis. The relation of the foregoing data to the theory of adrenalin-cholin antagonism is discussed.—G. V.

Subcutaneous calcifications in a case of PLURIGLANDULAR insufficiency. Pontoppidan (B.), Hosp.-Tid. (Copenhagen), 1921, **64**, Dermatol. Soc. Reports, 12-13.

A woman, aged 35, showed signs of **myxedema** and **sclerodermia.** During the last half-year there appeared under the skin in different places small tumours, which perforated and which contained masses of calcium phosphate, corresponding to the "granulomes calcaires sous-cutanées" of Milian.—K. H. K.

PLURIGLANDULAR syndrome with visceral inversion (Sindrome pluriglandolare in soggetto con inversione splanchnica total). Rossi (A.), Radiol. med. (Torino), 1916, **3**, 20-23.

Reference verified from Index Medicus.

(ENDOCRINOLOGY) The influence of the parasympathetic nerve toxins upon blood sugar and adrenalin hyperglycemia. Saito (I.), Keio Igaku, **1**, No. 10; abst., Jap. Med. World (Tokyo), 1922, **2**, 50.

In experimental studies it was found that stimulation of the peripheral ends of the parasympathetic nerves resulted in a decrease of the sugar content of the blood. Hyperglycemia following administration of pilocarpin is not the result of the nerve stimulation, but of central asphyxia. The parasympathetic nerves have no important relation to blood sugar since atropin sufficient to paralyze the peripheral structures causes no change. The hyperglycemia following a large quantity of atropin is due to stimulation of the nerve centers. The sympathetic and the parasympathetic nerves are antagonistic in their influence on carbohydrate mobilization. Adrenalin hyperglycemia may be depressed by pilocarpin or eserin.

—R. G. B.-R. G. H.

Biological remarks on constitution, ENDOCRINE ORGANS, internal metabolism and ions (Enkele biologische opmerkingen over constitutie, inwendige secreten, inwendige voeding, isoionie). de Somer, Geneesk. Jaarboek v. Vlaanderen (Gent), 1922, **2**, 195-201.

A short general review in which the author concludes that practically nothing is known of "constitution" or of endocrinology and that our knowledge on these subjects could be increased by a special study of colloids, electrolytes, and ions and their physicochemical properties.—J. K.

On the specificity of GASTRIN and pancreatic SECRETIN. Luckhardt (A. B.), Henn (S. C.) & Palmer (W. L.), Am. J. Physiol. (Balt.), 1922, **59**, 457-458.

The presence of gastrin in the duodenal mucosa, liver and thyroids raises a doubt as to the physiological significance of this substance previously described as present in the gastric mucosa. Gastrin is prepared from the duodenal mucosa in much the same way as is pancreatic secretin, and it seemed desirable to determine whether gastrin stimulates not only the stomach but also the pancreas, and whether pancreatic secretin could be prepared from gastric mucosa as well as intestinal, and stimulate both pancreas and stomach to secretory activity. In dogs, the stomachs of which, provided with gastrostomies, were ligated at the cardia and pylorus,

and which, in addition, possessed pancreatic fistulae and jejunostomies, the deep muscular injection of gastrin prepared from gastric or intestinal mucosa induced a pronounced secretion of gastric juice and a marked secretion of pancreatic juice. In such animals pancreatic secretin preparations, however made, stimulated not only the pancreas but greatly increased the volume and acidities of the gastric juice. There is no specificity of the so-called gastrins and secretins.—T. C. B.

A case of unilateral GIGANTISM. Monrad (S.), Ugesk. f. Læger (Copenhagen), 1921, **83**, 1375-1376.

The author previously (1911, 1914) demonstrated 5 cases of unilateral gigantism and has later seen 3 other cases, one of which is described. In a girl, aged 11 months, the parents noticed difference between the extremities from the age of 3 months. The patient now shows very marked gigantism of the right side, especially of the forearm, nates and hip, and of the right side of the face and right labium majus. The tongue is symmetrical. X-ray plates show hypertrophy of muscles and subcutaneous tissue, but not of the bones. The ossification centres and epiphyseal lines are normal and symmetrical. There is no disturbance of the sella turcica. Pupils, hair, sweat, temperature, sensibility, reflexes and galvanic reactions are normal and symmetrical. The **blood sugar** is normal. There are no rickets, but slight symptoms of lymphatic diathesis, and slight eosiniphilia. Of the 8 cases he has observed (3 boys and 5 girls) 4 were right sided and 4 left sided. Only in one case were the bones hypertrophied. In 6 cases the disease was congenital. In one case the gigantism was noted at the age of 2 years in connection with a nephrectomy for adrenal sarcoma.—K. H. K.

New views on the etiology of GLAUCOMA (Nuove vedute sulla etiologia del glaucoma). Paltracca, Riforma med. (Napoli), 1921, **37**, 763.

The author believes that glaucoma is due in old people to an imbalance brought about by depressed production of hypotensive hormones, especially those of the testis and the ovary. The result of his observations follow. In young subjects (25-40 years) glandular therapy, either per os or by instillation, resulted in no modification in the intraocular tension, but always proved successful after the climacteric. In subjects with unilateral glaucoma, modifications of tension were noticeable only in the healthy eye. It is supposed that the glaucomatous eye failed to react on account of pathological adhesions. After iridectomy, opotherapy helped to keep the intrabulbar tension low.—G. V.

(GONADS) Genetic and clinical study of five cases of hereditary-familial eunuchoidism (Studio di genetica e di clinica sopra

cinque casi di eunucoidismo eredo-famigliare). Furno (A.), Riv. di patol. nerv. (Firenze), 1922, **26**, 245-284.

Five cases of eunuchoidism in three generations in one family are described. The author's conclusions are as follows. (1) There is a form of hereditary-familial eunuchoidism, clearly distinguished from the forms of direct transmission from father to son, which necessarily are only slight spurious forms of hypogenitalism. (2) The hereditary-familial form, which is "dominant," usually mendelizes. The female sex appears to transmit the abnormality. (3) Four distinct forms of enunuchoidism are found, which can be classified as follows: (a) simple deficiency or absence of genital glands; (b) gerodermic eunuchoidism, in which the pathological hormonic influence of **thyroid** and **hypophysis** is added to congenital hypogenitalism; (c) **acromegalic** eunuchoidism, in which the pathological hormonic influence of the hypophysis complicates the congenital hypogenitalism; (d) eunuchoid feminilism, in which the congenital hypogenitalism is accompanied by a probable influence of heterosexual hormones from **ovarian** elements (endocrine hermaphroditism). (4) Pure eunuchoidism is therefore a monoglandular syndrome; the other clinical varieties are pluriglandular. (5) The gerodermic and acromegalic varieties of eunuchoidism and feminilism are not such from birth, as is the case with pure eunuchoidism, but develop during the puberal period. (6) Libido may appear, but it is tardy and does not last. (7) There is no constant finding in regard to vagotonia or sympatheticotonia in eunuchoids. (8) Grafting of cryptorchidic testes, rich in interstitial substance, is the best treatment; opotherapy gives negative results. When the grafts survive, the morphology and the psyche improve to normal, with the exception of the generative power. Even should the graft be absorbed general improvement results.—G. V.

(GONADS) Dystrophies and infantilism in chronic appendicitis of children (Distrofie ed infantilismo nelle appendiciti croniche degli adolescenti). Cignozzi (O.), Riforma med. (Napoli), 1922, **38**, 55-58.

Cignozzi reports several cases of chronic appendicitis, accompanied by infantilism and genital dystrophy in young people. After operation striking improvement of these conditions was seen.

—G. V.

(GONADS) Pubertas praecox combined with hermaphroditism. Collet, Ugesk. f. Læger (Copenhagen), 1921, **83**, 937.

The author mentions a case of precocious puberty and hermaphroditism in a child, aged 1½ years, in whom a removable tumor of the adrenal cortex was found.—K. H. K.

(GONADS) The independence of the seminal gland and the secondary sexual characters in fish (Sur l'indépendance de la glande séminale et des caractères sexuals secondaires chez les poissons. Étude expérimentale). Courrier (R.), Compt. rend. Acad. d. sc. (Par.), 1922, **174**, 70-72.

Spermatogenetic division in the testes of the winter-stickleback is activated by heat (keeping the fish in running water at 17° C.) and seminiferous ampullae are obtained having a structure completely identical with those present in the fish in summer. The seminal gland, under this treatment, qualitatively and quantitatively the same as at the mating period, does not, however, produce the appearance of secondary sexual characters, especially the special secretion of the kidney, although this organ is under the same conditions of temperature and nutrition as in summer. The two secondary sexual characters of the stickleback do not therefore react in the same fashion to the sexual hormone. The difference appears to be quantitative. A smaller amount is capable of influencing the chromatophores.—A. T. C.

(GONADS) Influence of castration on respiration, nutrition and fasting (Influence de la castration sur les échanges respiratories, la nutrition et le jeune). Heymans (C.), J. de physiol. et de path. gén. (Par.), 1921, **19**, 323-331.

Total castration diminishes the metabolism of the cock in normal nutrition from 20 to 30%. Partial nodular castration, although it conserves the morphological aspect of the bird, diminishes the respiratory exchange some 15%. This excess of metabolism of the normal cock over that of the castrate is considered as a secondary sexual characteristic. Fasting reduces the respiratory metabolism within 3 days to that of the castrated animal. The resistence to inanition of the cock is much lower than that of the castrate.—F. S. H.

(GONADS) Pubertas praecox in relation to tuberculous sclerosis. Krabbe (K.), Ugesk. f. Læger (Copenhagen), 1921, **83**, 1284.

Short description of two cases of tuberculous brain sclerosis combined with pubertas praecox in boys, aged 5 years and 13 years. The cases were described in detail in L'Encéphale (Paris), 1921.
—K. H. K.

(GONADS) Alimentary atherosclerosis in castrated animals (rabbits). Murada (K.), & Katsaka (B.), Nisshin Igaku, 1918, **8**, 1321-1340.

Alimentary atherosclerosis was more marked in castrated animals than in controls. This is attributed to the hypercholesterinemia which exists in castrated animals, which results in the

deposit of both neutral and doubly refractile fat in the walls of the vessels. The anatomical changes were practically identical with those of human atherosclerosis. The greater prevalence of atherosclerosis in Europeans than in Japanese is attributed to their meat diet.—L. G. K.

(GONADS) Comparative haemolysin formation in male and female rabbits. Ohnara (K.), Chuo Igakki Zasshi, 1918, No. 276, 1387-1388.

The pregnant female rabbit, and castrated females formed more hemolysin than did normal males, or non-pregnant normal females. This, the author attributes to the cessation of the internal secretion of the ovaries.—L. G. K.

Radioexcitation of the GONADS (Radioeccitamento delle ghiandole sessuali). Pais (A.), Riforma med. (Napoli), 1921, **37**, 1136.

By exposure of the sexual glands to minimal doses of x-rays increase of the spermatozoa has been obtained as well as acceleration of delayed puberty with amenorrhea.—G. V.

(GONADS) Sexual desire and internal secretion (Geschlechtstrieb und innere Sekretion). Weil (A.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 188-189.

Description of two cases. (1) A woman of 24 with powerful muscles, strength and intelligence. When she was 23 she lost some drops of blood from time to time, but she has never had a real menstruation. The labia majora are small; the labia minora, large; the clitoris is small. The uterus and ovary cannot be palpated. She is very intelligent but has no sexual desire. (2) A man of 35 without any growth of beard. At 20 years he had never felt any sexual desire, but married for social reasons. In the beginning of his marriage he sometimes felt sexual desire but it soon disappeared. He is very tall with a typical eunuchoid habitus. He has few pubic hairs and otherwise, no hairs on the trunk. His larynx is defectively developed. His scrotum is large, but his testicles, extremely small. He is extraordinarily intelligent.—J. K.

HYPOPHYSEAL syndrome (Syndrome hypophysaire). Achard (C.) & Rouillard (J.), Bull. et. mém. Soc. méd. d. hôp. de Par., 1922, **46**, 562-566.

A case report with no novel data.—F. S. H.

(HYPOPHYSIS) A case of dystrophia adiposo-genitalis (Un caso di distrofia adiposo-genitale). Albertario, Pediatria, (Napoli), 1921, **29**, 659.

A report of a case of dystrophia adiposo-genitalis in a boy 12 years old, whose father is diabetic and whose mother has gout;

there is also tuberculosis on the mother's side. No abnormality of the sella was found nor extra-hypophyseal cerebral lesions. The condition followed pertussis when the child was 4 years old. The author considers the case as a functional dystrophy of the hypophysis as shown by high tolerance of carbohydrates and insists on the interrelation of this condition with arthritism, diabetes and obesity. Pituitary and thyroid medication improved the patient very much.—G. V.

HYPOPHYSEAL disease. Askgaard (V.), Hosp.-Tid. (Copenhagen), 1919, **62**, Neurol. Soc. Report, 8.

A boy, 14 years old, suffered during the last year from thirst, attacks of headache and vomiting. He presented an infantile character, and was somewhat adipose. His genital organs were like those of a boy of 6 or 7 years. Urine output was 1700-2240 cc. Blood sugar was normal. The symptoms pointed to pituitary disease.
—K. H. K.

The morphogenesis of the HYPOPHYSIS in the tailed amphibia. Atwell (W.), Anat. Record (Phila.), 1922, **23**, 8.

Data given more completely elsewhere.

Lethargic encaphalitis with marked polyuria. HYPOPHYSEAL polyuria and pithiatric polyuria. (Encéphalite léthargique avec polyurie extrême. Polyurie hypophysaire et polyurie pithiatique). Benard (R.), Bull et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 553-557.

Report of a case of polyuria of 17 to 22 L. per day responding to pituitary treatment and psychotherapy.—F. S. H.

Two peculiar cases of tumor of the HYPOPHYSIS (Due no tevoli casi di tumori dell'ipofisi). Ceresole (G.), Riforma med. (Napoli), 1921, **37**, 668.

Radioscopy showed in one subject a tumor involving the anterior pituitary, penetrating the sphenoidal sinus, while the anterior clinoids were destroyed. In the second subject, the tumor had developed posteriorly with destruction of the posterior clinoids and of the lamina quadrilatera, but without lesions of the sphenoidal sinus. Radiotherapy was of no avail in the first case, but in the second, brought a great improvement in the soporous condition, the genital field, the papilla and the headaches.—G. V.

(HYPOPHYSIS) Pituitrin in obstetrics. Cleveland (C. H.), N. Orl. M. & S. J., 1922, **74**, 701-704.

A general discussion of the indications and contra-indications for the use of pituitrin. Conservatism is advised.—R. G. H.

The relation of the HYPOPHYSIS to anitbody production. Cutler (E. C.), J. Exper. M. (Balt.), 1922, **35**, 243-257.

The author undertook to determine whether the hypophysis plays any part in the development of resistance to infection. Guinea-pigs were employed as the experimental animals and the serum reactions of typhoid agglutination, hemagglutination and hemolysis were studied. In one series of animals the hypophysis was partially removed by a special method devised for this study, after which the immunological tests were made. In a second, the immune reactions were first developed, after which hypophysectomy was done, while in a third, animals were immunized, then fed continuously pituitary extract or given repeated injections and their titers subsequently determined. Normal and control operative animals were used throughout. None of these procedures, aiming to disturb the normal function of the hypophysis, had the slightest effect on the immunological reactions.—I. M.

Experimental echinococcosis of the posterior lobe of the HYPOPHYSIS. Hypophyseal lesion of infundibular origin (Echinococcose expérimentale due lobe postérieur de l'hypophyse. Lésion hypophysaire d'origine infundibulaire). Dévé (F.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 95-97.

Histological description of an echinococcus cyst of the hypophysis (posterior lobe) previously noted (Compt. rend. Soc. de biol. April 23, 1921).—T. C. B.

Pituitary nanism with tumor in the HYPOPHYSEAL region. Faber (K.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 1956-1962.

History of a man aged 17 years with nanism, genital dystrophy, polyuria and thirst, optic atrophy and contraction of the visual fields. On the right side was both a nasal and temporal defect; on the left a small nasal defect. Radiography showed the sella turcica normal, but above this there was an intense shadow, probably from a calcified tumour. The disturbances of the visual fields pointed to a process in the chiasma region. Hypophysine treatment was without effect.—K. H. K.

Variations of the blood pressure following injection of HYPOPHYSIN in different morbic conditions of infants (Le variazioni della pressione sanguigna in seguito ad iniezione di ipofisina in vari stati morbosi dell'infanzia). Fabris (S.), Pediatria (Napoli), 1921, **29**, 548-557.

The researches have been made in children from a few months to 12 years old. One cc. of "endo-ipofisina" of the Ist Sierotherp. Milanese was injected; the effect was studied on 52 children. It was found that the variations of pressure resulted in every case in

from 10 to 15 minutes after the injection. All children similarly affected offered an identical type of reaction, no matter what their age. The change of pressure was never more than 1 cm. (Pachon). The maximum and minimum variations ordinarily ran parallel, but in cases of bronco-pneumonia decrease of the maximum synchronized with a rise of the minimum pressure. The reaction lasted, on the average, 75 minutes, after which the pressure became normal. In most cases the minimum became normal before the maximum. In 13 cases the increase was preceded by a lowering (almost all cases of latent tuberculosis, nephritis or diabetes insipidus). In 15, steady increase of pressure was shown after the injection (scrofula, exudative diathesis, tracheo-bronchial adenopathy, cerebral tuberculoma). In 22, a paradoxical reaction was noted, namely, a steady, slow decreasing of the pressure (mitral stenosis, polyuria, bronco-pneumonia, kalazar, tuberculous peritonitis, pleuro-peritonitis, lymphatism). The author feels that an extension of such observations may lead to important diagnostic criteria, both as regards organic lesions and hormone balance.—G. V.

(HYPOPHYSIS) Acromegaly from late hereditary lues (Sindrome acromegalico por heredo lues tardia). Gazzolo (J. J.), Prensa méd. argentina (Buenos Aires), 1921, **8**, 259.

A 28 year old patient complained of headaches and dizziness. The hands and feet were slightly large, the features somewhat acromegalic. Hereditary syphilis is regarded as the causal factor because of a positive Wassermann reaction, pigmented scars of the limbs, and slight aniscoria. Amelioration followed mercurial treatment. The skull was not radiographed.—B. A. H.

Clinical study of hypertrophy of the HYPOPHYSIS during pregnancy (Klinischer Beitrag zur Schwangerschaftshypertrophie der Hypophyse). Jung (P.), Schweiz. med. Wchnschr., 1922, **52**, 61-62.

Jung points out that the diagnosis of enlargement of the hypophysis during pregnancy largely depends upon the x-ray picture. Usually a marked enlargement of the sella turcica occurs, characterized by a distinct outward curve. The hypophyseal hyperplasia is rarely so marked as to induce a clinically perceptible condition. Two pertinent cases are cited from the literature and these are followed by a detailed description of the author's case. The author believes that in such cases a primary disease of the hypophysis exists, simulating an adenoma. During pregnancy this hypophyseal condition acquires a certain growth stimulus which disappears after the termination of pregnancy, leading to the retrogression of the hypertrophy. The pressure on the optic chiasm is decreased and the visual disturbances diminish.—C. P. McC.

Researches on the normal and pathological structure of the pharyngeal HYPOPHYSIS (Ricerche sulla struttura normale e patologica

della ipofisi faringea). Lunghetti (B.) R. Accad. d. fisiocritici. in Siena, 1920; abst., Pathologica (Genova), 1922, **13,** 58.

The pharyngeal hypophysis, which is almost constant in man, is otherwise seen among vertebrates only in some birds (gallinacea) and carnivora. It is formed, especially in man, of glandular tissue, structurally similar to that of the pars tuberalis of the hypophysis. It is supposed that the pharyngeal hypophysis, though within narrower limits, has a function similar to that of the anterior lobe; and it can be inferred that, owing to the presence of parenchymal cords, pavement epithelium and vacuolizations, it may give origin to blastomata. In inflammations of the pharynx as well as of the pharyngeal tonsil it may undergo alterations, as is the case with the anterior lobe. This can be explained by the strict relations (topographic, vascular) with the pharyngeal tonsil and mucosa. Owing to this it may show hyperemia, connective septa thickened or infiltrated with leukocytes, and various alterations of the parenchyma. The anterior lobe, also, may undergo congestion and accentuated fluctuations in its chromophil elements, colloid and enclosed cells. On account of the frequency of such alterations in several diseases the author is in doubt whether the anterior lobe should be incriminated in cases giving pituitary symptoms without thoroughly excluding the possibility of the pharyngeal hypophysis being at fault.—G. V.

HYPOPHYSIS and ADRENAL changes in fetal pseudo-hermaphroditism (Sulla presenza di cellule simil-gravidiche nell'ipofisi, di formazioni ghiandoliformi nella corteccia surrenale e di altri fatti degni feto pseudoermafrodita). Pelligrini (R.), Riforma med. (Napoli), 1917, **32,** 1089-1123.

Reference verified from Index Medicus.

Hirschsprung's disease and HYPOPHYSEAL nanism (Morba di Hirschsprung e nanismo ipofisario). Samaja, Pediatria (Napoli), 1922, **30,** 35-36.

Report of a case of nanism in a girl of 20, whose mother's stature is below normal. The sella turcica of the patient is very small and the anterior and posterior clinoids joined. She has enlarged esophagus, megacolon and megarectum. Samaja advances the hypothesis that if the post-pituitary constantly secretes pituitrin it should exert a steady influence on the contraction of the smooth fibres of the intestine. Through deficiency of this action, once a congenital hypertrophy of the circular fibres is given at a certain point, dilatation through stasis may occur and a consequent hypertrophy of the longitudinal fibres above the obstacle.—G. V.

Tumor of the HYPOPHYSIS presenting clinical manifestations very similar to retrobulbar neuritis. Tone (S.), Chuo Kanka Iho, **13,** No. 3; abst., Jap. Med. World (Tokyo), 1921, **1,** 20.

The author observed a very interesting case of pituitary tumor in a male, 45 years old, who complained of difficulty of vision in both eyes.—R. G. B.

Anatomical modifications of the HYPOPHYSIS after removal of the thyroid (Sulle modificazioni anatomiche dell'ipofisi degli animali stiroidati). Vallillo (G.), Boll. d. Ist. steroterap. Milanese, 1920, 213-223; abst., Pathologica (Genova), 1922, **13**, 55.

The histological observations on the prehypophyseal parenchyma of goats and horses previously deprived of the thyroid show modifications, on the whole equal in all cases. These modifications are characterized by increase of the eosinophil cells, or by their regressive alterations. The presence of new elements determines the increase in the weight of the gland. There was found no relation between the condition of the hypophysis and the length of time elapsing after the removal of the thyroid. It is concluded that the eosinophil tissue increases through a process of restitution, which, as happens in analogous cases, may go beyond the normal. This hypothesis explains the macroscopic and the microscopic findings. In the animals discussed it has not been found that the combined action of the regressive and progressive phenomena on the hypophyseal parenchyma causes hypertrophy.—G. V.

Pathological findings in the HYPOPHYSIS and PARATHYROID glands. Harbitz, Forh. med. Selsk. i Kristiana, 1916, 20-25.

Reference verified from Index Medicus.

Clinical case of pathological dissociation between the two lobes of the HYPOPHYSIS (Caso clinico di dissociazione patologica fra i due lobe dell'ipofisi). Samaja (N.), Riv. sper. di Freniat. (Reggio-Emilia), 1920, **44**, 540-564; abst. Pathologica (Genova), 1922, **13**, 56.

The author found a case of moderate **gigantism** (without symptoms of eunuchoidism or other endocrine insufficiency) complete at 16 years of age. The subject showed an exaggerated tolerance for carbohydrates and relative oliguria. The earlier manifestation was one of hyperfunction of the anterior lobe, the second, of hypofunction of the posterior lobe. The hypertrophy of the anterior lobe in the restricted space apparently caused first irritation of the posterior lobe with subsequent pressure atrophy. Such a functional dissociation has been observed, even if not explained, in regard to **acromegaly**. In a case of Falta's the alimentary glycosuria was positive in the beginning but later, negative. W. Schlesinger and Borchardt published a similar case and recently Cushing has discussed analogous cases. In Borchardt's case the diabetes lasted 5 years, but afterward no glycosuria could be provoked with 150 gm. of glucose. Polyuria is also a transitory phenomenon in acromegaly. In the

first period, therefore, the proliferative process of the anterior lobe, which causes acromegaly, irritates the posterior lobe, producing glycosuria and spontaneous diabetes; afterward the posterior lobe atrophies and the exaggerated tolerance of carbohydrates follows alimentary glycosuria.—G. V.

The importance of the HYPOPHYSIS in the etiology of diabetes mellitus (Ueber die Bedeutung der Hypophyse in der Pathogenese des Diabetes mellitus). Vernon (O.), Zentralbl. f. allg. Path. u. path. Anat. (Jena), 1921, **31**, 521-531.

This work, from the Pathological Institute of the University of Jena, is largely a speculation, to some extent based on the anatomical studies of six cases of diabetes mellitus. The absence of anatomical lesions in the islands of Langerhans in many diabetics is noted, also the vast literature involving other glands of internal secretion with sugar tolerance and metastasis. Of these, he selects the hypophysis. Experimental workers have reported glycosurias accompanying injury or removal of the anterior lobe and the increased tolerance for sugar associated with injury or removal of the posterior lobe. Lowered tolerance and glycosuria is frequently seen in acromegaly. "Heute wissen wir, dass diese Erkrankung (Akromegalie) auf einer Ueberfunktion des Hypophysenvorderlappens beruht" (!) No systematic anatomical studies on the hypophysis in diabetes have previously been recorded. Six cases with autopsy findings are reported, in three of which no lesions of the pancreas or islands of Langerhans could be found. One that developed, following a fall from a scaffold, was clinically diagnosed as traumatic diabetes, and autopsy showed necrosis of the stalk of the pituitary. The second was a long standing, mild case of exophthalmic goitre in which there was moderate enlargement of the anterior lobe of the hypophysis (eosinophilic type). A third was a case of carcinoma of the lung (bronchial type), in which the posterior lobe of the hypophysis was nearly destroyed by metastasis. While the experimental work does not entirely convince one that there is a relation between diabetes and the hypophysis, it seems to show that hyperfunctioning of the anterior lobe and stimulation of the posterior lobe can cause glycosuria. There are cases of diabetes mellitus in which the pathological findings suggest hypophyseal origin, as in the case with traumatic necrosis and tumor destruction of the normal connection of the hypophysis with the brain.—D. M.

Case of true INFANTILISM. Klein (J.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 899-908.

A woman, aged 25 years, showed a typically infantile aspect: height 124 cm.; weight 35 kg.; no development of mammae; no pubic or axillary hair; open epiphyseal lines (radioscopically); very infantile psyche; slight lymphocytosis. There was a slightly deform-

ing tuberculous spondylitis. The case was considered by the author as one of true infantilism. There were no other endocrine signs. —K. H. K.

(LIVER) The cardio-accelerator agent produced by hepatic stimulation. Cannon (W. B.) & Griffith (F. R.), Am. J. Physiol. (Balt.), 1922, **59**, 480.

The accelerator effect on the denervated heart of stimulating the hepatic nerves is not due to the failure of the liver to protect the heart from substances absorbed from the intestinal canal, for blood drawn from the hepatic veins during stimulation will accelerate the heart when injected into the inferior vena cava. As a rule the effect is most marked during the digestion of meat. It seems probable that a substance of special and unknown nature is discharged into the blood stream when the hepatic nerves are excited.—T. C. B.

Variations of the hematic reaction to LYMPHOGANGLINE (Sopra alcune variazioni del reperto ematico prodotte dalla Linfoganglina con speciale riguardo alla eosinofilia). Mazzarella (A.), Riforma med. (Napoli), 1921, **37**, 1103-1104.

The article is a preliminary note on the action of lymphatic ganglia extract, which increases the number of the white corpuscles, but modifies the formula by inducing mononucleosis and eosinophilia. The eosinophilia differs from that produced by serum or excitation of the vagus (pilocarpin). The experiments are said to confirm the observations of Marfori and Chistoni that lymphogangline has a hormonic action antagonistic to **adrenalin**.—G. V.

LIPODYSTROPHY. Askgaard (V.), Hosp.-Tid. (Copenhagen), 1921, **64**, Neurol. Soc. Report, 18-19.

A woman, aged 33, showed very marked emaciation of the face and thorax, contrasting strongly with very voluminous nates, hips and legs.—K. H. K.

Two cases of MACROGENITOSOMIA from internal hydrocephalus with a note on the differential diagnosis of hydrocephalis and on the question of repeated ventricular puncture (Zwei Fälle von Makrogenitosomia ex Hydrocephalo interno, zugleich ein Beitrag zur Differentialdiagnose des Hydrocephalus und zur Frage der wiederholten Ventrikelpunktion). Gàbschuss (G.), Monatschr, f. Kinderh. (Leipz. & Wien), 1922, **22**, 574-586.

Two cases of macrogenitosomia praecox are reported in girls, aged 9 and 9½ years, respectively. In both there was premature development of the external genitalia and the breasts, but menstruation had not appeared. Neurological disturbances were present in both; they were relieved by trepaning and repeated ventricular punctures. There was no evidence of tumor and the author reports both

children as having internal hydrocephalus. He believes this to be responsible for the general bodily changes, perhaps by pressure on the hypophysis or pineal with resultant endocrine disturbance.
—C. H. G.

MONGOLISM of possibly abortive form in congenital heart disease. Krabbe (K. H.), Bibliot. f. Læger (Copenhagen), 1919, **3**, 70-76.

The author describes a case of congenital heart disease which showed some slight signs of mongolism, namely, epicanthus, deviation of the 5th finger, retarded physical development, hypotonia, and slight retardation of ossification. The patient did not show such marked idiocy as that of the ordinary mongolian type. The existence of abortive forms of mongolism should be considered, especially in cases of congenital heart disease. In accordance with most modern authors, Krabbe considers mongolism as due to a general deficient fetal development, not as an endocrine disease.—K. H. K.

The rôle of the LUTEIN cells of the OVARY in certain uterine hemorrhages (Du role des cellules lutéiniques de l'ovaire dans certaines hémorrages utérines). DeRonville (G.) & Sappey (P.), Gynéc. et obst. (Paris), 1922, **5**, 1-38.

Clinical and histological report of 12 cases of ovarian and menstrual disturbances. The conclusions are that menstruation is due to the internal secretion of the ovary formed by the lutein cells, either the interstitial cells of the theca interna or the cells of the corpus luteum. Hyperfunction of these structures produces pathological hemorrhage. Amenorrhea is the result of hypofunction.
—F. S. H.

(MAMMA) Lactation and menstruation (Laktation und Menstruation). Engel (S.), Monatschr. f. Kinderh. (Leipz. & Wien), 1922, **22**, 545-551.

The author discusses the prevalent views as to the effect of menstruation on lactation. He also presents curves showing the total daily milk secretion in two wet nurses. No change in the form of these curves occurred with the reappearance of menstruation. Engel accepts the view that the reappearance of the menstrual flow follows the failure of the mammary secretion and is not the cause of the failure as is commonly supposed.—C. H. G.

The OVARY and the endocrinologist. Frank (R. T.), J. Am. M. Ass. (Chicago), 1922, **78**, 181-185.

The development of the sexual duct systems (Wolffian and Mullerian ducts) and of the secondary sex characters are qualitatively and quantitatively governed by the sex glands. The transformation of the infantile genital tract, inclusive of the secondary sex characters, to the adult stage results from a quantitative increase in

ovarian secretion. Menstruation signifies the abortion of an unimpregnated ovum. The "interstitial gland," as emphasized by Meyer, does not exist in the human female. Frank calls attention to the work of Iscovesco, Herrmann and others on the lipoidal bodies contained in corpus luteum, which produce uterine hyperemia and hyperplasia. Hypoplasia of the female duct system (vagina, uterus, tubes) results from insufficient ovarian action. He, contrary to many investigators, considers other factors, such as the pituitary, of no importance in this connection. He laments the fact that today we have no better ovarian extract on the market than we had in 1910 and considers the "degreased" or "defatted" commercial preparations pharmacologically inert.—E. N.

The CORPUS LUTEUM (Contribuzione allo studio del corpo luteo). Gaifami, Riforma med. (Napoli), 1921, **37**, 1136.

No original data. It is denied that the corpus luteum has any influence in determining extrauterine pregnancy.—G. V.

(OVARY) Therapy and pathogenesis of osteomalacia (Contributo clinico alla terapia e patogenesi dell'osteomalacia). Gentili (G.), Riforma med. (Napoli), 1922, **38**, 97-98.

Report of two cases of osteomalacia during and following pregnancy, which have been treated with "Ovarial" (Calcium phosphate and ovarian extract). From the very satisfactory results obtained in both cases Gentili infers that osteomalacia is due, not to hyperfunction of the ovaries, but to dysfunction of these glands. The "Ovarial" was given in doses of from 20 to 30 drops before each meal for one or one and a half months, followed by a rest period of fifteen days.—G. V.

Swelling of the MAMMA in new born infants (Über die Milchdrüsenschwellung bei Neugeborenen. Zugleich über extramedelläre Blutbildung). Gruber (G. B.), Ztschr. f. Kinderh. (Berlin), 1921, **30**, 336-362.

A well illustrated study of the histological changes associated with the swelling of the mammary glands in new born infants. Not of immediate endocrine interest.—C. H. G.

(OVARY) Morphological and physiological studies on the musculature of the mature Graafian follicle of the sow. Guttmacher (M. S.) & Guttmacher (A. F.), Johns Hopkins Hosp. Bull. (Balt.), 1921, **32**, 394-399.

The ovaries were promptly immersed in Bouin's fluid. After fixation, and the usual paraffin embedding technique, the tissue was sectioned at from 3.3 to 5 micra. The sections were then stained in haemotoxylin with iron alum as a mordant. After decolorization they were subjected to the Van Gieson technique for the differen-

tiation of smooth muscle and connective tissue fibers. For the study of the nerve supply, good results were obtained by Ehrlich's methylene blue staining, following the modifications of J. G. Wilson. The method is fully described. The authors found an abundance of smooth muscle cells in the theca externa. Autonomic nerves with typical motor endings occur in juxtaposition to these cells. The musculature of the ovary and its follicles has a double innervation, the true sympathetics acting as inhibitory and the parasympathetics as excitatory nerves. The innervation is similar to that of the intestinal musculature. The authors were not able to demonstrate rupture of the follicles by producing contractions of the muscle fibres, but they feel that they have demonstrated that rupture of the follicle is not produced solely by an increase in the arterial tension of the follicular vessels.—E. M.

CORPUS LUTEUM extract in the treatment of the vomiting of pregnancy. King (E. L.), J. Am. M. Ass. (Chicago), 1922, **78**, 484-486.

A report of 48 cases of vomiting of pregnancy. Of these, 12 were treated with extract of corpus luteum; ten received corpus luteum only, while 2 received ovarian extract, also. Nine were treated with ovarian extract alone. Twenty-eight received the usual treatment of sedatives, gastric lavage, colonic irrigations of sodium bicarbonate, forced fluids, glucose, etc.; two of this group were also given horse serum, with negative results. From this experience, the author cannot share Hirst's enthusiasm over the corpus luteum treatment. True, some mild cases were cured, but the same may be said of any other line of treatment. He criticizes adversely the theory on which Hirst bases this form of treatment.—E. N.

MENSTRUATION and the swelling of other organs (Menstruation und Wellenbewegung). Labhardt (A.) & Hüssy (P.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttg.), 1922, **84**, 715-741.

Biological experiments on guinea-pigs demonstrated an extragenital swelling of various organs synchronous with the sexual cycle. The high point of this swelling occurs in the pre-gravid state or the beginning of menstruation. Its origin is in the monthly preparation for pregnancy. Its first phase is anabolic and is necessary for the increased activity of the organism. This is followed by a catabolic phase, if the ovum is not fertilized, and a decrease in activity of the whole body. Menstruation, as such, is only a symptom of a general swelling. The important phase is the pre-gravid. A good review of current data is included.—F. S. H.

Hypertrophy of fragments of the OVARY in partial castration (Sur l'hypertrophie des fragments ovariens dans la castration partielle). Lipschütz (A.), Wagner (C.), & Tamm (R.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 240-242.

Carmichael and Marshall have shown that ovarian fragments in the rabbit undergo remarkable hypertrophy. The authors in a series of experiments have verified this. The hypertrophy is caused exclusively by the entering into follicular development of a relatively large number of ovules.—T. C. B.

Relation of corpus luteum to menstruation and pregnancy. Mackenzie (W. R.), Brit. M. J. (Lond.), 1922, **i**, 343-344.

A report of five operative cases which lead the author to conclude that injury to either a true or false corpus luteum will simulate a ruptured extrauterine gestation, that injury to a true corpus luteum will bring on an abortion, and that rupture of a false corpus luteum will bring on menstruation and its accompanying ovulation.
—E. N.

The antagonistic action of the OVARY on ADRENALIN glycosuria. Mochizuki (K.), Nikon Fujinka Gakkwai Zasshi, **16**, No. 9; abst., Jap. Med. World (Tokyo), 1922, **2**, 46.

The author concludes that the ovary and adrenal glands act antagonistically on carbohydrate metabolism.—R. G. B.

(OVARY) The change in blood sugar after castration (I Communication.) Nakanarinmi (S.), Keio Igaku, **1**, No. 7; abst., Jap. Med. World (Tokyo), 1922, **2**, 15.

The author estimated the blood sugar in young and old female rabbits whose ovaries had been extirpated. There was a marked rise in blood sugar which was hastened by the injection of adrenalin hydrochloride. An injection of ovarian extract rapidly brought the hyperglycemia approximately to normal. When a combination of adrenalin and various extracts was injected into a castrated rabbit with blood sugar changes and into a normal rabbit, the same changes were obtained in both. This would imply that the accelerated chromophilic action could be depressed by the administration of ovarian extract.—R. G. B.

(OVARY) Chronological and causal relations between labor, ovulation and menstruation (Zeitiche und kausale Beziehungen zwischen Geburt, Ovulation und Menstruation). Novak (J.), Centralbl. f. Gynäk. (Leipz.), 1921, **45**, 1697-1699.

The author presents a very interesting hypothesis as to the cause of the onset of labor. He calls attention to the striking fact that the first menstrual period in the non-lactating woman as a rule makes its appearance six weeks after labor. This would indicate that labor occurs at the time of an ovulation, for the latter is known to take place about midway between the periods. He believes that ovulation during pregnancy is inhibited by the corpus luteum and later by the placenta, but that this restraining influence is removed

toward the end of pregnancy. He mentions various clinical facts in support of his hypothesis, which would be considerably strengthened, as he himself says, were it possible to demonstrate recently ruptured follicles in the ovaries of women dying in labor.—E. N.

MENSTRUATION and its anomalies. A critical compilation of the literature of 1915 to 1918 (Der Menstruationszyklus und seine Anomalien. Das Ergebnis der kritisch zusammengestellten Gesamtliteratur der Jahre 1915, 1916, 1917, 1918). Schroeder (R.), Monatschr. f. Geburtsh. u. Gynaek. (Berl.), 1920, **53**, 207-251.

This is an excellent and quite exhaustive review of the general subject by one who has himself been one of the most industrious workers in the field. The subject is considered under seven headings, viz.: (1) The anatomy of the menstrual cycle; (2) the cause of the menstrual cycle; (3) the physiology of the menstrual cycle; (4) too early and too late menstruation; vicarious menstruation; results of castration; climacterium; (5) amenorrhea; (6) dysmenorrhea; (7) meno- and metro-rrhagia.—E. N.

The influence of CORPUS LUTEUM extract on erythropoiesis in artificially anemic rabbits (Ueber den Einfluss von Corpus Luteum-Extrakt auf die Erythropoese bei künstlich anämisierten Kaninchen). Rothlin (E.), Arch. f. d. ges. Physiol. (Berl.), 1922, **193**, 102-108.

Anemia was produced by bleeding. Subcutaneous injection of extract had no effect. Feeding desiccated corpus luteum had no effect on females; on males there appeared to be a favorable effect. There was no definite alteration in the color-index.—A. T. C.

OVARIAN lipoids (Sui lipoidi contenuti nell'ovaio). Serono (C.) & Palozzi (A.), Folia Med. (Napoli), 1916, **2**, 34-41.

Reference verified from Index Medicus.

Internal secretion of the OVARY and osteomalacia (Cellule a secrezione interna dell'ovaja ed osteomalacia). Spirito (F.), Riforma med. (Napoli). 1921, **37**, 1137.

From his personal observations the author objects to the statement of Wallart that hypertrophy of the interstitial ovarian tissue may be a factor in osteomalacia.—G. V.

Lipoid metabolism of CORPUS LUTEUM (Metabolismo lipoide del corpo luteo). Tricomi (E.), Riforma med. (Napoli), 1921, **37**, 762.

According to a series of observations of Tricomi on the corpus luteum of the cow it appears that the amount of fat increases from the first days to the fifth month, then it decreases, to increase again

from the seventh month on. The fat is nearly all lipoid the first two months; its amount does not increase with the increase of fat, but diminishes after the third month to almost total disappearance at the end of pregnancy.—G. V.

Experimental researches on the effect of removal of the OVARY, ADRENALS and THYROID during pregnancy (Ricerche sperimentali intorno all'asportazione dell'ovaia, surrene, tiroide rispetto all'andamento della gravidanza). Sirtori (C.), Riv. crit. di med. (Firenze), 1919, **20**, 358.

Bilateral ovariectomy in the first days of pregnancy as well as destruction of corpus luteum (by chemical means, in situ) always leads to abortion. During the first half of pregnancy ovariectomy nearly always has the same effect, while within a few days of conception, destruction of corpus luteum "in situ" allows pregnancy to proceed. In the second half of gestation neither type of interference causes abortion. Bilateral ovariectomy and subsequent grafting of ovaries into the peritoneum does not interrupt the pregnancy. Unilateral adrenal ablation in the first days induces abortion, while bilateral ablation causes abortion on the first or second day and death within three days. At a later period unilateral adrenal destruction proves harmless, but should both ovaries be removed in addition, death occurs before abortion. Partial thyroidectomy in the first days leads to abortion, while no effect results in a later period. The author claims that the hormones of the foetus may act on the mother.—G. V.

Studies of the centrally conditioned changes in blood sugar and the influence of the internal secretion of the OVARY on this reaction, together with a new proof of the internal secretion of the ovary (Beiträge zu Physiologie der Drüsen. LII. Untersuchungen über zentral bedingte Veränderung des Blutzuckergehaltes und über den Einfluss des inneren Sekretes des Ovariums auf diese Reaktion zugleich ein neuer Nachweis der inneren Sekretion des Ovariums). Takakusu (S.), Biochem. Ztschr. (Berl.), 1922, **128**, 1-31.

The blood sugar changes were studied on normal and castrated female rabbits after the injection of theobromine sodium salicylate. It was found that the hyperglycemia produced as the result of the administration of this compound became less as the interval between the loss of the ovaries and the test increased. The drug hyperglycemia is supposed to be centrally conditioned because the sensitivity of certain parts of the central nervous system is reduced after loss of the ovarian hormone. When a castrated rabbit is parabiotically joined with a normal animal the reaction to the drug is increased, but it is decreased after disjunction. This is taken as a proof of a circulating ovarian hormone. The removal of the ovaries results in marked atrophy of the uterus and vagina. The decrease in the

hyperglycemia induced by the drug after ovariectomy is specific for the sex, since testicular extirpation is not followed by a similar phenomenon. Castration does not change the reaction of rabbits to heat puncture.—F. S. H.

Precocious MENSTRUATION and mammary organotherapy (Mestruazioni precoci e opterapia mammaria). Tronconi (S.), Morgagni, 1921, —, —, No. 27; Abst., Terapia (Milano), 1921, **11**, 18.

Report of a six year old girl, whose mother is affected with **goiter.** The girl shows precocious puberal development and has menstruated. To stop a flow, which was rendering the patient anemic, the usual medication was of no avail. Mammary gland tablets were given with satisfactory result. The author compares this case with that of an infant of 16 months whose vaginal flow (not cyclic) was due to an ovarian tumor; in this case neither **pituitary** nor mammary gland had any effect. The author insists on the importance of mammary therapy for diagnostic as well as for therapic purposes.—G. V.

Lipoids in the human OVARY (Lipoide im Menschlichen Ovarium). Weishaupt (E.), Monatschr. f. Geburtsh. u. Gynaek. (Berl.), 1922, **56**, 276-282.

A histological study of the lipoids of ovaries from man, guinea-pigs, rabbits and one rat.—F. S. H.

The significance of the CORPUS LUTEUM in connection with Fraenkel's theory. Yochelman (T.), Mag. Lond. (Roy. Free Hosp.) School Med. f. Women (Lond.), 1916, **11**, 41-47.

Reference verified from Index Medicus.

DYSMENORRHEA. Young (J. V. D.), N. York M. J., 1921, **114**, 395-397.

Of no endocrine interest, except for a highly speculative hypothesis as to the causation of dysmenorrhea.—E. N.

The internal secretion of the PANCREAS. Banting (F. G.), Best (C. H.) & Macleod (J. J. R.), Am. J. Physiol. (Balt.), 1922, **59**, 479.

A neutral or faintly acid extract of the pancreas, degenerated after duct ligation, was prepared, and its effect on pancreatic **diabetes** investigated. Ten weeks after ligation the gland was removed and extracted with ice-cold Ringer's solution. Injection of this extract invariably caused a marked reduction of sugar in the blood and urine. Extracts of liver, spleen and boiled pancreas had no effect. Subcutaneous injections had a less rapid but more sustained effect than intravenous.—T. C. B.

Internal secretion of the PANCREAS in pregnancy (Richerche istologiche e fisiopathologische sulla secrezione interne del pancreas in gravido). Falco (A.), Ann. di ostet. (Milano), 1916, **1**, 1-16.

Reference verified from Index Medicus.

Acute hemorrhagic PANCREATITIS. Henrichsen (J.), Hosp.-Tid. (Copenhagen), 1919, **62**, 353-360.

A woman, 38 years old, showed acute peritoneal symptoms, resembling those in peritonitis of perforation. The existence of severe glucosuria, however, pointed to pancreatic disease. Laparotomy was performed, but the result was fatal after 3 weeks. Autopsy confirmed the diagnosis: acute hemorrhagic pancreatitis.—K. H. K.

The rôle of the PANCREAS in assimilation. Paulesco (N. C.), Arch. internat. de physiol. (Liége & Par.), 1921, **17**, 85-109.

The injection of a pancreatic extract into the jugular vein of a depancreatized dog may produce a transitory diminution or even suppression of the hyperglucemia, which may be followed by a hypoglucemia and the transitory diminution or suppression of the glucosuria. Moreover a decrease in the blood and urinary urea and acetone is observed. This effect begins immediately after the injection, reaches its maximum in about 2 hours, and persists for about 12 hours. It varies with the amount of pancreas used in preparing the extract. When a pancreatic extract is similarly injected into a normal dog there occurs a decrease in the **blood sugar** and blood urea as well as in the urinary urea. The intravenous injection of physiological serum, or of organs other than the pancreas, such as the spleen, or into the spinal canal of Na nucleinate which produces fever, fails to bring about the results described above.

—Chem. Abst., **16**, 580.

Relation between the PANCREAS and the eyes (Rapporti fra pancreas ed occhio). Reitano (D.), Folia Med. (Napoli), 1916, **2**, 319-347.

Reference verified from Index Medicus.

Further examinations of the PINEAL gland in mammals. Krabbe (K. H.), Det kongelige danske videnskabernes selskabs biologiske meddelelser (Copenhagen), 1921 (III), **7**, 1-30. (Résumé in French.)

The author, who formerly has described the pineal gland embryologically and histologically in a series of mammals, has continued these examinations in Echidna, Didelphys, Onychogale, Tamandua, Myrmecophaga, lemur and Nycticebus, and in fetuses of Lobodon and Leptonychotes. In Echidna the structure is like that in many other mammals, especially Chiroptera and Insectivora. In

marsupials there are two different types; in Didelphys the organ is very primitive; in Hypsirrymnus, well developed. In Elephas the pineal is small and shows a follicular structure, otherwise not found in mammals. In Tamandua, Myrmecophaga and Choloepus the organ is absolutely missing as it is in Dasypus. The pineal in the higher apes resembles in some cases that of the marsupials, in others that of the lower apes. The embryological examinations in seals confirms what the author has found before in Phoca embryos. On the whole, the author has found a relative uniformity of the pineal in Echidna, some marsupials and insectivores, the higher and some of the lower apes. This type shows a rounded, slightly flattened or slightly oval form. The organ consists of uniform cells with rounded nuclei and scanty protoplasm, without discernable cell boundaries (pineal cells). Between the pineal cells are found a smaller number of glia-cells. The organ is ordinarily well vascularized. From this type the organ deviates in rodents, in which it is very long and thin; in seals, in which it is enormously vascularized; in horses, pigs, goats and men, in which there is a great deal of connective tissue; in ungulates, in which there are enormous glia; in men and higher apes in which there are many nervous elements. It is rudimentary in edentates and very small in whales and elephants.—K. H. K.

The relation of PARATHYROID tetany to intestinal bacteria. Dragstedt (L. R.), Am. J. Physiol. (Balt.), 1922, **59**, 483.

There is considerable evidence that certain types of tetany are associated with gastro-intestinal disturbances. This may be a toxemia due to putrefactive bacteria. Depending on the degree to which an aciduric or fermentative flora can be maintained, the toxemia can be prevented. An aciduric intestinal flora was produced in six young dogs by a diet of bread and milk, and milk ad libitum plus 25 gms. of lactose daily. The animals lived for ten days after parathyroidectomy, and at no time developed tetany. In a series of ten adult dogs an aciduric intestinal flora was maintained by a diet of boiled rice, beef heart and lactose. Parathyroidectomy was then done, and the feeding continued. Corresponding to the degree to which an aciduric flora could be maintained, tetany was prevented. "The experiments indicate a direct relation between parathyroid tetany and intestinal intoxication, and lend support to the view that the function of the parathyroids is in part the removal or neutralization of toxic substances in the blood." As the animals died even when protected from tetany, the latter symptoms may be but a part of a profound metabolic derangement.—T. C. B.

Treatment of paralysis agitans by transplantation of animal PARATHYROIDS (Beeinflussung der Paralysis agitans durch Ueberpflanzung von tierischer Nebenschilddrüse). Jakob (A.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 113.

Kuhl has stated that grafting a parathyroid may have a splendid effect in Parkinson's disease, but the same effect is obtained by systematic exercises. The disease is not due to hypoparathyroidism, but to unknown defects of the corpus striatum and the pallidum. —J. K.

(PARATHYROIDS) Tetanoid neuroses. Levison (P.), Ugesk. f. Læger (Copenhagen), 1921, **83**, 1259-1268.

The author gives a short description of 7 cases, which he considers as "formes frustes" of **tetany.** Nervousness, paresthesia in fingers and toes, slight loss of hair and slight Trousseau's and Chvostek's phenomena were observed. Treatment with calcium was followed by marked improvement.—K. H. K.

(PARATHYROIDS) Clinical studies on tetany (Klinische Studien zur Tetanie). Melchoir (E.), Mitt a. d. Grenzgeb. Med. u. Chir. (Jena), 1921, **34**, 400-436.

The parathyroids play an important part in the pathogenesis of tetany. Calcium metabolism is changed in this disease as well as in rickets and in osteomalacia, and pathological changes have been found in the parathyroids in rickets and osteomalacia. During pregnancy the nervous irritability is generally increased, the parathyroids get more blood and show an increased number of chromophil cells, while the body loses calcium. From these facts it can be seen that a relation between osteomalacia, rickets and tetany is probable; this is in accordance with the author's statement of two years ago (Berl. klin. Wchnschr., 1919, p. 837) that the large number of cases of osteomalacia after the war would probably be accompanied by a large number of cases of tetany. The number of cases of postoperative tetany has markedly increased during the last years. One would be inclined to believe that this is due to a change in the technic of strumectomy (strumectomy totalis, ligation of the four arteries), but the author proves that in clinics where this technic is not used, more cases of tetany are also seen than before the war. It is much more probable that feeding during and after the war is the chief cause of the high number of cases. The administration of calcium lactate and parathyroid tablets sometimes has a good effect. This treatment should be tried before parathyroid transplantation because this will not always give good results. Another important point in tetany is that spasms are not always the cause of death. In postoperative and in spontaneous tetany spasms may disappear after treatment, but the patients die in coma parathyreopriva. It is possible that in some of these cases tetany of the heart, as described by Ibrahim, is the cause of death, but in others, an intoxication may be responsible for the coma. There have been cases in experimental tetany where no spasms occurred but where the patients or the animals gradually became dull and died in coma, during which the

facialis and Trousseau's symptoms were positive. The abdominal organs may also show tetanic symptoms. Tetany of the bladder has repeatedly been described; spasms of the stomach (x-rays of which are published in this article) are seen, though not frequently. An attack of cholelithiasis has been regularly compared with an attack of tetany. Tetany may also be caused by stenosis of the pylorus, lues, peritonitis or appendicitis.—J. K.

Hyperplasia of the PARATHYROID glands in rickets. Minor (J.) & Pappenheimer (A. M.), Proc. N. York Path. Soc. (N. Y.), 1921, **21**, 98-102.

Published elsewhere.

The significance of the PLACENTA, particularly the trophoblast, for the duration of pregnancy and the onset of labor (Die Beudeutung der Plazenta, insbesondere des Trophoblastes, für die Schwangerschaftsdauer, und den Geburtseintritt). de Snoo (K.), Monatschr. f. Geburtsh. u. Gynaek. (Berl.), 1922, **57**, 1-26.

Report of several cases in which desiccated placenta was administered in various amounts. The author concludes that the internal secretory function of the placenta rests in the trophoblast, because its origin and development is so closely associated with the growth of the fertilized ovum and its morphological alterations. Since the article is mainly speculative the details are unnecessary. —F. S. H.

Effect of PROSTATECTOMY on integration of muscular movements of the white rat. Macht (D. I.) & Ulrich (J. L.), Am. J. Physiol. (Balt.), 1922, **59**, 482.

A study of the effect of prostatectomy on muscular coordination and efficiency by means of the "rope problem." White rats were trained to cross a room on a tightly stretched rope, starting from a platform at one end, and going to a platform containing food at the other end. At first they could not cross, but after repeated trials learned to do so rapidly, and without slipping off. After training there was a marked improvement in strength and tonus of the entire musculature. Two sets of experiments are described. In the first the rats were trained and then prostatectomized. After recovery they were quickly retrained, and no change in muscular integration was apparent. In the second group the rats were prostatectomized after a few trials on the rope, and after recovery training was again begun. It was noticed that this second group learned very poorly, compared to the first group, and even after a much longer period they could not run over the rope in perfect fashion. Progress was slower and more difficult. The muscles showed tremblings and the hind legs were weak. Feeding dried prostate caused marked improvement.—T. C. B.

QUINCKES' EDEMA in the Danish medical literature. Faber (K.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 448-449.

The author notes that Christoffersen's case (Endocrinol., **3**, 385) was not the first in the Danish literature. Cases have been reported by Lange, Dreyer, Strandgaard and Rasch.—K. H. K.

Function of the SPLEEN (Beiträge zur Physiologie der Drüsen. LIII. Die Funktion der Milz, insbesondere bei normalen und erhöhtem Sauerstoffbedarf). Bernet (E.), Biochem. Ztschr. (Berl.), 1922, **128**, 250-267.

Working with rabbits the author found that no increase in ammonia excretion occurs during increased oxygen want. When the spleen is removed a change in the ammonia excretion may take place, but this is not influenced by increased oxygen demand. Splenectomized rabbits excrete more nitrogen in the urine than do normal rabbits. This signifies an increased protein decomposition when the spleen is removed and leads to the idea that this organ has a regulatory influence on metabolism in the sense of a sparing action. When the oxygen demand is increased in splenectomized rabbits the nitrogen excretion is also increased. Pneumothorax was the means employed to produce an increased oxygen demand.—F. S. H.

(SPLEEN) Recent investigations on internal secretions (Osservazioni in toro ad alcune recenti ricerche nel campo delle secrezioni interne). Patta (A.), Boll. d. Soc. med.-chir. di Pavia (Milano), 1919 (No. 4); Abst., Pathologica (Genova), 1922, **13**, 60.

The intravenous injection of venous blood from the normally appearing spleens of normal animals led to diminished blood pressure and pulse rate, followed after a few minutes by normal or even elevated pressure. Even a greater amount of blood from a small, hard spleen with thickened capsule did not cause any modification either of pressure or of the pulse.—G. V.

Influence of local application of TESTICLE substance on cicatrization (Il processo di cicatrizzazione delle piaghe sotto l'influsso di applicazioni del parenchima testicolare). Ajevoli (E.), Riforma med. (Napoli), 1921, **37**, 947-949.

A summary of the findings of Voronoff and Bostwick in their experiments of pancreas, thyroid, adrenal and testis as topical application on sores. The author takes occasion to recall his experience, published in the Riforma med., 1890.—G. V.

Report of a case of cyst of the TESTICLE in a dog. Barach (A. L.), Proc. N. York Path. Soc. (N. Y.), 1919, **19**, 38-50.

This is a report of a careful study of a case of cyst of the testicle which followed trauma in a dog, with a discussion of the patho-

genesis of non-retention cysts. The article has a special interest for pathologists, but no immediate endocrine interest.—J. P. S.

Pathological changes in the TESTES in constitutional diseases, particularly marasmus (Pathologisch-anatomische Veränderungen der Keimdrüsen bei Konstitutionskrankheiten, im besonderen bei der Pädatrophie). Jaffe (R.), Frankfurt. Ztschr. f. Path. (Wiesb.), 1921, **26**, 250-267.

This study was made in the Pathological Institute, University of Frankfurt. The author points out that autopsy findings in marasmus are generally negative. From a study of the testes in normal children and in marasmus he comes to the conclusion that the most certain criterion for the anatomical diagnosis in children's testes is the number of interstitial cells and their fat content. In the testes of normal children one finds very little connective tissue, the interstitial cells are few and either contain no fat or at most only traces of fat. In chronic infectious diseases there may be a secondary atrophy. In such cases one finds the stroma between the seminiferous tubules increased and edematous; the interstitial cells show no change from normal. In children with a clinical diagnosis of constitutional inferiority, one notes a definite increase in the connective tissue stroma and in the interstitial cells, both in number and in lipoid content. These are the changes usually found in children with marasmus. The increase of interstitial cells and their fat content is not looked upon as a cause of the condition but rather as the manifestation of constitutional inferiority.—D. M.

(TESTES) Experimental retardation of masculinization (Ralentissement expérimental de la masculinisation). Lipschütz (A.), Wagner (C.) & Bormann (F.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 238-240.

Horizontal incisions were made into the testicles of a rabbit two months ago. On the right side the incision was made into the epididymis, on the left side, not. The control rabbit born the same day attained puberty at the age of four months and a half; the other, not until about seven and a half months. The histology of the testicles is given.—T. C. B.

(TESTES) Vasecomy in a dog as a regeneration experiment. Sand (K.), Ugesk. f. Læger (Copenhagen), 1921, **83**, 1509-1516.

The case is described of a dog, aged 12 years, very senile, emaciated and miserable. For a time after vasectomy on the left side and resection of epididymis on the right, the dog remained very miserable, but after 3-4 weeks it improved markedly. The movements became more rapid, the hair grew better, the appetite increased and the dog regained its earlier vigor.—K. H. K.

Urethral malformations accompanied by TESTICULAR anomalies (Sulla concomitanza di alcune malformazioni uretrali con anomalie testicolari). Torraca (L.) Riforma med. (Napoli), 1921, **37**, 1093-1095.

Not of endocrine interest.—G. V.

Sudden death of two children in the same family. THYMIC death in hereditary syphilis (Morte improvvisa di due babini nella stessa famiglia. Sulle morti timiche in eredoluetici). Battino (C.), Pediatria (Napoli), 1922, **30**, 248-256.

The author reports a case of a girl, 6 years old, whose brother at the age of 4 had died suddenly. There was psychasthenia on her father's side and tuberculosis on her mother's. No hereditary syphilis showed in the children. Two brothers were living and apparently well. All of them were well nourished but pale. The girl, apparently well, after a hearty meal at home, ate again with a sound appetite a few hours after. Suddenly, without any symptom, she fell dead. Autopsy disclosed nothing abnormal in the abdomen except congestion and distension of the stomach and intestines. Upon opening the thorax a thymus was found of the length and width of the sternum, but without cysts, gummata or hemorrhages; there were no signs of compression. The lymphatic system was rather well developed. Since there was no cyanosis or spasm of the glottis, the author believes that, if the death be ascribed to nervous inhibition, the sympathetic fibres to the thymus might have been involved rather than the sensory nerves of the trachea. Anaphylactic shock due to hypersecretion of the thymus seems more likely to have caused the death. A positive Wassermann test was later obtained in both parents.—G. V.

Anatomical and pathological study of the THYMUS in infancy (Contributo allo studio anatomico e pathologico del timo nella prima età). Canelli (A. F.), Pediatria (Napoli), 1921, **30**, 58-64.

The author has studied the formation of "Gitterfasern" in normal and in pathological cases. In patients with normal thymi the following conclusions were reached. In the first five months of intrauterine life only a few of these fibres can be found either in the cortex or in the medulla, and these mostly around the vessels. From birth to 3 years of age the "Gitterfasern" are not much more numerous, yet the perilobar reticulum is more evident and some fibrillae from the reticulum and from the perivascular sheets proceed toward the parenchyma. From 4 to 15 years of age they become numerous,—more so at the periphery than in the central part in both the cortex and medulla, but they are never seen either around or in the Hassel's corpuscles. After the 16th year of age they become quite predominant, especially in the cortical part, but some are also found around the Hassal's corpuscles, especially if calcified.

In adipose degeneration when the distinction between cortex and medulla almost disappears they are quite numerous in the fatty tissue. They are lacking in the cords of epithelial cells, except around vessels or in the connective formations. From this the author infers that their lack in the epithelioid tracts evidences the epithelial nature of these tracts. In patients with pathological thymi, without distinction of age, the "Gitterfasern" are greatly developed.—G. V.

(THYMUS) Caseated thymona of the mediastinum. Cleland (J. B.) & Beare (F. H.), Med. J. Australia (Sydney), 1922, **1**, 182.

A case report. The tumor was 6.2x5x3.7 cm.; it reached almost to the base of the neck and was firmly adherent to the aorta. It was largely necrotic but showed areas of typical thymus tissue. Aside from the tumor no gross abnormality was found.—R. G. H.

THYMIC and pseudo-thymic stridor (Stridore timico e stridori pseudotimici). Cozzolino (O.), Pediatria (Napoli), 1921, **29**, 729-743.

The article is a discussion on the various conditions, besides enlarged thymus, which may provoke stridor. A number of thymic cases greatly improved by radium therapy is reported.—G. V.

(THYMUS) A case of Erb-Goldflam's disease (Su di un caso di morbo di Erb-Goldflam). D'Amato (L.), Riforma med. (Napoli), 1921, **37**, 1204.

In connection with a case report D'Amato mentions that he has found that the removal of the thymus gland of myasthenics may result in damage to the function and the structure of the muscles. —G. V.

A case of THYMOMA. Ewing (J.), Proc. N. York Path. Soc. (N. Y.), 1919, **19**, 156-160.

Of no immediate endocrine interest.—J. P. S.

A case of THYMOMA. Klingenstein (P.), Proc. N. York Path. Soc. (N. Y.), 1919, **19**, 151-156.

Of no immediate endocrine interest.—J. P. S.

A tumor of the THYMUS gland. Rohdenburg (G. L. L.), Proc. N. York Path. Soc. (N. Y.), 1920, **20**, 97-99.

Of no immediate endocrine interest.—J. P. S.

Chronic inflammation of the THYMUS. Schmorl, Gesell. f. Naturf. u. Heilk. (Dresden), 1919; Abst., Pathologica (Genova), 1922, **13**, 34.

The author reports a case of chronic thymitis in an infant 9 months old who did not show any symptom of it while living. There was no rickets. The patient had undergone tracheotomy nine days before and the author concludes that even in so short a time thymic lesions could have formed.—G. V.

THYMUS tumors (I tumori epiteliali del timo; di un caso de adenoma del reticolo timico). Vanzetti (F.), Arch. per le sc. med. (Torino), 1917, **40**, 264-307.

References verified from Index Medicus.

Lymph follicles with germinal centers in the THYMUS medulla (Ueber Lymphfollikel mit Keimzentren im Thymusmark). Wegelin (C.), Centralbl. f. allg. Path. u. path. Anat. (Jena), 1918, **29**, 441-447.

The author refers to reports in the literature in which definite lymphoid tissue was reported in the medulla of the thymus, especially in **Graves' disease**, and reports the case of an eleven year old girl, operated on in the Surgical Clinic at Bern, in which a large goiter together with the cervical portion of the hyperplastic thymus was removed. There were many clinical manifestations of **status thymicolymphaticus.** He believes that the presence of germinal centers in the thymus medulla is very rare, but that they may actually occur in both the hyperplastic thymus of Graves' disease and status thymicolymphaticus. He then discusses whether the lymphoid elements of the thymus are entirely epithelial or of mixed epithelial and lymphatic origin. His studies support the views held by Hammar, Maximow and Hart that the small thymic cell originates from migrated blood and lymphoid elements.—D. M.

Auto-transplantation of the THYMUS in the spleen of rabbits (Uber autoplastische Transplantation der Thymus in die Milz bei Kaninchen). Yamanoi (S.), Frankfurt. Ztschr. f. Path. (Wiesb.), 1921, **26**, 356-381.

The author reviews some of the literature on both homio- and auto-transplantation of the thymus and points out the failure of all homiographs. The results reported were obtained on thirty rabbits, mostly adults, as young rabbits did not withstand the operative procedures well. Various sites have been used for transplanting the thymus, but the author selected the spleen, introducing the thymic tissue immediately after its removal by means of a trocar and stylet. He obtained the thymic tissue by dividing the sternocleidomastoid muscles, pulling up the thymus and amputating part of it. The effect, therefore, of a thymic deficiency on the life history of the graft was not studied. He studied the transplants microscopically from 1 day to 163 days after implantation. In only three animals did the transplants survive longer than 100 days. He found the usual de-

struction of the transplanted thymic tissue during the first few days. On or after the fourteenth day definite regeneration of thymic cells was found; this included Hassall's corpuscles and the true small cortical lymphocytes. He was not able to study the fate of the transplanted thymic eosinophil in this material, but has undertaken another series of experiments to investigate this point. The theories of origin of the small cortical thymic cells are discussed, i. e., whether they arise from epithelial elements, as Stöhr and others have claimed, or from the blood and lymphoid tissue as Hammar, Maximow and others hold. He supports the view that these small thymic cells are derived from the epithelial thymic elements. Abstracter's Note: It is doubtful whether the spleen offers the best site for the study of tissue transplants from bone marrow, lymph glands or thymus.—D. M.

Treatment of emesis with THYROIDINE. Albeck (V.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 44-46.

The author has formerly found that most cases of emesis are complicated with very small thyroid glands. He has therefore tried to treat a number of cases of emesis with thyroidine. In cases of slight severity results were not marked enough to consider, but 20 very severe cases which were treated with thyroidine, 15 cgm., every day, showed a very marked improvement. Some were completely cured.—K. H. K.

The relation between emesis and the size of the THYROID, and demonstration of a strange modification of the thyroid in sows with young. Albeck (V.); Ugesk. f. Læger (Copenhagen), 1919, 1047-1054, 1083-1087.

The author has observed that there is a constant relation between the cases of emesis and the size and consistency of the thyroid; women with a large and soft thyroid never have emesis during pregnancy, while women with a small, hard thyroid always have emesis. In 23 cows with young the author found the weight of the thyroid to be 4.57 gm per 100 kg. body weight; in cows without young, 4.35 gm. In 34 sows with young the weight of the thyroid was 14.58 gm per 100 kg., in 163 sows without young, 15.65 gm. In 3 sows with eclampsia the weight was 12.31 gm., but the individual variations were too great to permit conclusions. Histological examinations showed that the thyroids in sows with young were modified from the 3d to the 4th week. In the middle of pregnancy the organ showed complete adenomatous structure with very many and very small follicles, with cubical or cylindrical epithelium, often in several layers. At the end of pregnancy these modifications disappeared. The modifications are different from those in rabbits and guinea-pigs described by Engelhorn, but they are like the changes in cats described by Borzystowsky.—K. H. K.

(THYROID) The cause of cretinism (Sulla causa del cretinismo). Allara (V.), Attualità med. (Milano), 1916, **5**, 432.

Reference verified from Index Medicus.

(THYROID) Etiology of endemic goiter and cretinism (Nuove vedute sull'etiologia del gozzo endemico e del cretinismo). Arcangeli (U.), Studium (Napoli), 1916, **9**, 65-70.

See Endocrin., **1**, 103.

(THYROID) Diagnosis and therapy of Graves' disease. Bang (S.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 20-26.

It is very difficult to compare statistics on Graves' disease, especially since some authors believe that exophthalmos is always present, while others find it in only 50-70%. The author warns against too inclusive use of the term "Graves' disease." Perhaps the method of Krogh will help in a more exact diagnosis. The author recommends beginning with hygienic-dietetic treatment, to be followed by x-ray therapy. In the cases that are not cured by this treatment, operation is recommended.—K. H. K.

(THYROID) Etiology of goiter (Per il quesito etiologico del gozzo). Bertarelli (E.), Morgagni (Milano), 1916, **58**, 693-696; Riv. d'ig. e san. pubb., 1916, **27**, 481-485.

Reference verified from Index Medicus.

(THYROID) Infantile mongolianism (Mongolisme infantile). de Biehler (M.), Arch. de méd. d. enf. (Par.), 1922, **25**, 81-89.

A general discussion of the clinical symptomatology of mongolian idiocy in infancy. Four cases are reported in brief. In two a slight improvement was noted following the administration of thyroid extract in doses of 0.05 gm. thrice daily.—C. H. G.

(THYROID) Common types of goiter. Bram (I.), Penn. M. J. (Harrisburg), 1922, **25**, 336-345.

Clear differential pictures are presented of the types of nontoxic and toxic goiter. Special emphasis is placed on the proper recognition and differentiation of toxic adenoma, as distinguished from hyperplastic goiter (exophthalmic goiter, Graves' disease). There is a concise tabulation of the principal signs and symptoms, history and course of these two common thyroid disorders. The various diagnostic tests for toxic goiter are commented upon. The differential blood count, Harrower's thyroid extract test, complement fixation test, hyperglycemia test, mydriasis test, pituitary test and adrenalin hypersensitiveness test are not considered very valuable or reliable. The determination of the basal metabolic rate and

the author's quinine test are helpful and trustworthy. The prompt curative result of surgical procedures in toxic adenoma is admitted, but surgery is regarded as unwise, if not contraindicated, in the exophthalmic type.—H. L.

(THYROID) Congenital megacolon and myxedema (Megacolon congenito e mixedema). Cattaneo, Pediatria (Napoli), 1921, **29**, 661.

The author reports a case of congenital megacolon involving the ampulla and the descending colon. A condition of myxedema was found and thyroid medication prescribed. The myxedematous condition not only disappeared, but the constipation was cured, and a second x-ray picture taken after the treatment showed the descending colon normal. In cases of congenital megacolon the author insists on the necessity of looking for an endocrine disfunction.

—G. V.

(THYROID) Are there reliable criteria of operability in exophthalmic goiter? Cheever (D.), Arch. Surg. (Chicago), 1921, **2**, 21-36.

Cheever attempts a formulation of exact criteria of the ability of the thyrotoxic patient to withstand operation, stressing as contraindications acute exacerbations; muscular weakness; continued marked weight loss; serious organic visceral disease; enlarged thymus (present in 75% of exophthalmic cases) unless irradiation is effective in decreasing thymic activity; a basal rate of plus 30 or more; severe reactions after minor surgical procedures, such as injections into the gland, cauterizations or ligations. He believes the evidence supporting the contention of Means and Aub (Arch. Int. Med., Chicago, 1919, **24**, 645) that "vagotonic" syndromes offer greater vulnerability than those of the sympatheticotonic type, to be inconclusive. Unfortunately many factors concerned in the toxemia are not susceptible of accurate measurement; moreover, in hyperthyroidism, operations will always be attended by a peculiar factor of danger, not present in other operations which are technically similar.—C. R.

(THYROID) Handling of the toxic goiter under ether-oil colonic anesthesia. Dickinson (G. K.), Am. J. Surg. (N. Y.), 1922, **36**, 40-42.

Because of the emotional state in toxic goiter due to thyroid and adrenal activity, Dickinson endorses Crile's technique for "stealing the goiter," but substitutes ether-oil colonic anesthesia for nitrous oxide. His own results have been excellent, but he believes that the method should be more widely used and reported upon before it can be regarded as a proven procedure.—C. R.

THYROIDECTOMY and PARATHYROIDECTOMY with relation to the development of immune substances. Ecker (E. E.) & Goldblatt (H.), J. Exper. M. (Balt.), 1921, **34**, 275-294.

The authors attempted to determine the relation of thyroidectomy and parathyroidectomy to the development of immune bodies. They compared power of recovered thyroidectomized and thyroparathyroidectomized animals to develop anti-sheep hemolysin with that of normal animals. After thyroidectomy and partial parathyroidectomy in rabbits the average and maximum hemolytic titers of the sera were equal to, or higher than, those in normal animals injected with sheep blood in the same way. After complete thyro-parathyroidectomy a small proportion of the animals lived, even after developing very severe tetany. In these animals the anti-sheep hemolysin developed by the same technique was of a uniformily low titer,—on an average, one-fifth that of the controls.—I. M.

(THYROID) Cachexia strumipriva with marked ascites as dominant symptom. Faber (K.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 1403-1408.

From the age of 15 years a girl showed enlargement of the thyroid; at the age of 23 years strumectomy was performed. The goiter consisted predominately of colloid tumour and cysts. After the operation she was well for 2 years, then severe ascites set in with headache and loss of hair. The ascites receded after punctures. Laparatomy was performed to make possible a Talmas operation, but the liver and all the abdominal organs were found normal. After each paracentesis ascites recurred. In one year 11 punctures and two laparatomies were made. After treatment with thyroidine there appeared a very marked diminishing of the ascites. Upon discontinuation of the thyroidine ascites recurred, but disappeared completely when the thyroid treatment was renewed. Also the myxedematous symptoms disappeared. The author believes that the ascites is definitely to be ascribed to hypothyroidism, and as analogous with the thyroprivic edemata described by Eppinger. The ascitic manifestation appears to be unique, so far as the literature disclosed. Sodium chloride metabolism was found normal by the Strauss test.—K. H. K.

Abdominal and THYROID galvanization as a treatment of hyperthyroidism (La galvanisation abdomino-thyroidienne dans le traitement des syndromes d'hyperthyroidie). Foubert (F.), These de Paris, 1921.

Galvanization with electrodes on the abdomen and thyroid has a good effect in hyperthyroidism and in Graves' disease. The treatment has no contraindications and is absolutely without danger. The thyroid can stand a much stronger current without disagreeable symptoms than other parts of the body. Combination with

other treatment is possible and may even be advisable (for instance, x-rays). The effects on the tachycardia, the goiter, the exophthalmus and diarrhea are especially remarkable. Operation is indicated only in cases where even this treatment fails, which is very rare.—J. K.

Urticaria and HYPOTHYROIDISM (Orticaria ed ipotiroidia). Fubini (E.), Pathologica (Genova), 1922, **14**, 27-30.

Report of a case of urticaria lasting nine years in a woman 30 years old. She first menstruated at 18. She shows a complete syndrome of hypothyroidism; enophthalmus; small thyroid; tendency to adiposity; scarse, irregular menstruation; frigidity; dry skin and hair; characteristic eyebrow; brittle nails with white spots; easily acquired colds; several spells of bronchial asthma and a great sensibility to cold and hypothermia. Except for these symptoms the general examination was negative. She underwent years of treatments of all kinds, but found no relief except when treated with pluriglandular therapy, and this was but slight. The patient was then put on general diet and given injections of "endotiroidina." In a few days a remarkable improvement began, leading to a practical recovery. The author believes urticaria due to anaphylaxis, which, according to his opinion, may be induced by external protein as well as by protein formed in the organism. He is inclined to believe, also, that owing to the dysfunction of the thyroid abnormal proteins may be liberated from the thyroid giving origin to anaphylactic trouble, with analogous mechanism to hetero-proteins.—G. V.

The iodine content of the THYROID in the Japanese adult. Fukushima (T.), Nikan Naikagakkwai Zasshi, **9**, No. 5; Abst., Jap. Med. World (Tokyo), 1922, **2**, 45.

The author determined the iodine content of the thyroids of subjects free from any complication with thyroid disorders. He used the Bowman-Anten's color reaction test for iodine. He found that the total weight of the Japanese thyroid was one-third that in Europeans. It was equally distributed in the lobes, being 0.81 mg. per gram of fresh glands. The comparative iodine content appeared to be higher in the Japanese, possibly due to difference in the food. There was no distinction in iodine content of thyroid in patients with different diseases or diseases extending over varying periods. Generally considered, the iodine content of the thyroid varied more with the administration of iodine preparations, especially those given internally.—R. G. B.

(THYROID) Experimental goiter produced by fluorine (Goitre experimental par le flour). Goldemberg (L.), Semana méd. (Buenos Aires), 1921, **28**, 628.

The addition of 2-3 mg. sodium fluoride to the food of young white rats during a period of six to eight months produced chronic

intoxication with retarded growth, etc. The thyroid increased in size, its parenchyma became compact, with considerable cellular hyperplasia. The author considers that this enlargement amounts to experimental goiter.—B. A. H.

The influence of THYROID products on the production of myocardial necrosis. Goodpasture (E. W.), J. Exper. M. (Balt.), 1921, **34**, 407-423.

Finding acute necrosis of the cardiac muscle at autopsy in patients dying of myocardial exhaustion from hyperthyroidism, the author has studied the effect of desiccated thyroid and thyroxin in large doses to determine whether such hearts are more readily injured by toxic agents, such as chloroform, than normal hearts. Healthy young rabbits under standard conditions were given, in one series, 1 mg. of desiccated thyroid per day by mouth and, in another, 1 mg. of crystalline thyroxin intravenously every second or third day over a period of two to three weeks. A similarly treated series of animals was given, in addition, after the thyroid effects were fully developed, one hour of light chloroform anaesthesia. The clinical effects of the thyroid were marked in all cases, the pulse rate increasing about 50% and the weight decreasing markedly. When the animals were sacrificed at the end of two or three weeks, the series receiving thyroid products only showed no gross lesions and, microscopically, relatively insignificant changes only, in the form of perivascular fibrosis. The injury appeared to have been produced by the first doses given, with a subsequent attempt at repair. The second series, in which the animals received one hour of light chloroform anaesthesia 24 hours before being sacrificed, showed very definite focal necroses of the myocardium, both macroscopically and microscopically. Control animals showed no such changes with chloroform alone and the author concludes that a heart stimulated to abnormal activity by thyroid products is more susceptible to injury from poisons of acute infections, chloroform, etc., than is a normally acting heart.—I. M.

Hypoplasia of the THYROID in an infant (Hypoplastische Schilddrüse von einem Säugling). Graupner, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 144.

Demonstration of the hypoplastic thyroid of an infant who had enormously developed muscles.—J. K.

Tuberculosis with THYROID manifestations (Tubercolosi a manifestatzioni tiroidee—tireo-tubercolosi). Janowski, Riforma med. (Napoli), 1921, **37**, 344-345.

Report of an article published by Janowski in the Ann. de Med., 1921.—G. V.

Results on an enlarged THYROID gland nine years after obstructing the veins. Guthrie (C. C.), Am. J. Physiol. (Balt.), 1922, **59**, 447.

Following a short period of enlargement after ligation of all the major veins to the left lobe, it greatly diminished in size. The bitch was killed in a fight nine years after operation. The left lobe was subnormal in size, but showed normal appearing areas of thyroid alveoli and colloid. More fibrous tissue was present than normally.

—T. C. B.

(THYROID) Systematic goiter therapy and prophylaxis (Ueber systematische Kropf-Therapie und Prophylaxe). Hunziker (H.) & Wyss (M. v.), Schweiz. Med. Wchnschr., 1922, **52**, 49-54.

This report is based on some additional observations by Hunziker and Wyss on a group of 775 goitrous school children. Extensive tables, which indicate the relation of goiter incidence, size and decrease (under treatment) in relation to sex, height and weight, nodular formation, age, effects of vicarious treatment, etc., are given. For prophylaxis, potassium iodide is used. Preference is given to this salt rather than to organic compounds. Standardized doses of KI are not recommended. Better results are believed to have been obtained from doses adjusted to age, physical condition, size of goiter, geographic situation of affected groups, etc. The doses as used, approximated one mgm. of KI per week throughout the year. This procedure was found both to reduce goiters already existing and to prevent goiter formation in the normal individual. These authors conclude that both goiter prophylaxis and goiter therapy on a wide basis may be profitably carried out in schools.—C. P. McC.

The influence of THYROID preparations on the blood picture and especially on eosinophilic cells. Kamikozawa (Y.), Igaku Chuwo Zasshi (Tokyo), No. 349; Abst., Jap. Med. World (Tokyo), 1921, **1**, 18.

After thyroid extract was administered in 6 cases of bronchial asthma a decrease in the number of eosinophiles followed within 7-10 days and persisted over varying periods. There was a corresponding improvement in the pulmonary condition. In a few cases there was a slight increase in eosinophiles at the beginning, giving place later to decrease. In three cases of ankylostomiasis, a lowering in the number of white blood cells with a relative increase in polynuclear cells resulted. There was an absolute increase in eosinophiles. Similar conditions were seen in vagal eosinophilia. In normal patients thyroid caused no change in the eosinophilic count. Drugs increasing the tension of the sympathetic nerves cause an increase in polymorphonuclear neutrophilic and a decrease in eosinophilic cells, while those increasing the tension of the vagi produce an increase in mononuclear and eosinophilic cells.—R. G. B.

(THYROID) Technique of complement fixation in Basedow's disease. Koopman (J.), Proc. N. York Path. Soc. (N. Y.), 1921, **21**, 56-57.

The blood of some patients with symptoms of Basedow's disease binds complement in the presence of an antigen made from normal glands. To prepare the antigen, the glands of dogs are obtained under aseptic precautions as soon as possible after death. All extraneous tissue is removed and the gland is minced finely with sterile scissors. The mass of thyroid is weighed carefully and is then ground in a mortar with washed, sterilized sand and an amount of sodium chloride equal to one-tenth gram for each gram of gland used. A few drops of 2 per cent tricresol is added for each 10 grams of thyroid, and the mixture is bottled and kept in the icebox. For use, 10 cc. of distilled water is used for each gram of gland in the suspension of sand and ground thyroid. The sand and solid matter are removed by centrifugation. A mixture of thyroids from several dogs is recommended. This antigen, which necessarily contains much extraneous matter, deteriorates slowly and after about three weeks it is necessary to secure a new supply. The test is set up in the form of a titration, using a constant amount of the patient's serum, which is not more than one-fourth of the quantity which is anti-complementary. The antigen is used in varied amounts, beginning with an excess and ending with the least amount that can be expected to give fixation of complement. At the same time the anti-complementary titer of the antigen is determined by setting up a series of control tubes containing the same quantities of antigen as used in the test. The result is indicated by the difference between the quantity of antigen that is anti-complementary of itself and the quantity that binds complement in the presence of serum. A negative serum with antigen will often bind less complement than the antigen alone. A serum is considered positive when it binds complement in the presence of one-half or less than one-half of the anti-complementary dose of antigen, and the smaller the amount of antigen necessary for complete fixation the stronger the reaction. Fixation is carried out for from four to six hours in the icebox.

—J. P. S.

Three cases of vagotonia, complicated by irregular pulsation, with special reference to the influence of THYROID. Kozawai (Y.), Chugai Iji Shinpo (Tokyo), No. 995; Jap. Med. World (Tokyo), 1922, **2**, 47.

The author administered thyroid material to certain patients having irregular pulsation occurring with vagotonia. The first had Stokes-Adams' disease and typical vagotonia. The second had bronchial asthma and auriculo-ventricular pulsation. The third had exopthalmos and, after x-ray treatment, showed signs of vagotonia. In these three cases, thyroid administration was followed by remarkable results, for the symptoms either disappeared or were greatly

ameliorated. In the last case, eosinophilia was completely suppressed and the heart action improved. Thyroid preparation augments sympathetic activity and thus mitigates vagotonia. ("Vagotonia" is "strain of the vagus" in the abstract from which this is taken.—Ed.)—R. G. B.

(THYROID) Gastric secretion in Graves' disease. Kramer-Petersen, Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 46-48.

In 12 cases of Graves' disease the author found severe diarrhea in 7 and achylia or hypochylia in 10. There was no disturbance of the motor function of the stomach.—K. H. K.

Determination of the respiratory metabolism, especially in patients suffering from THYROID diseases. Krogh (M.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 3-7.

Diseases of the thyroid manifest themselves in the total energy changes. Respiratory metabolism serves as an index of these. In myxedema the metabolism may be diminished to 60%, in Graves' disease, increased 100%. Metabolism examinations are therefore necessary in thyroid diseases, especially in cases in which the diagnosis is uncertain or before thyroid operations. The examinations employed in the Mayo Clinic are somewhat difficult for the ordinary practitioner to employ; the gas analysis is difficult. The author therefore has made her examinations with a respiratory apparatus constructed by August Krogh. The patient respires in a registering spirometer in the bottom of which there is a box containing 8 kg. sodium hydrate and calcium hydrate. The inspired air passes under the box, the expired, over it. Before the examination the reservoir of the spirometer is filled with oxygen. The reservoir will sink during the whole experiment, while the patient absorbs the oxygen, and the carbonic acid is absorbed by the hydrates. The degree of filling of the spirometer and the respirations are registered on a rotating cylinder, moving 2cm. per minute. If the curve of respiration is irregular the result is without significance. The result can otherwise be calculated from the curve.—K. H. K.

Glande THYROIDE et anaphylaxie. Lauzenberg (A.) & Képinow (L.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 204-206.

A study of anaphylactic shock in animals deprived of the thyroid. Guinea pigs were thyroidectomized and kept for a week before beginning the experiment. Controls were chosen of the same weight. The sensitizing dose was subcutaneous; the anaphylactic, by the carotid. The lethal dose was 1 cc. of a tenth dilution serum. Eight thyroidectomized animals were sensitized on the day of the operation. Twenty days later they received a lethal dose of serum. All the controls died. Six of the thyroidectomized animals are still

living. Three had a slight dyspnoea, but none of them had anaphylaxis. Of the two that died, one was autopsied and a bit of thyroid was found, which may account for death. When only half of the thyroid was removed, all died, both experimental and control, with the classic symptoms of shock. In another series, the animals were sensitized and twenty days later the thyroids were removed. Twenty-seven days after sensitization the anaphylactic injection was given. Both groups died. To sum up, there was no anaphylaxis when thyroidectomy was done before sensitization. Removal of the thyroids after sensitization does not prevent shock. A later communication is promised.—T. C. B.

(THYROID) Eye symptoms in Graves' disease. Lindgren (E.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 36-44.

A discussion of the frequency of the different eye symptoms in Graves' disease.—K. H. K.

(THYROID) A case of myxoedema (Un caso di mixedema). Luzzatto (A.), Riforma med. (Napoli), 1921, **37**, 787.

A baby girl one year old showed from the 8th month of life myxoedematous appearance, prognathism, macroglossia, prominent abdomen and cyanosis of the limbs. Thyroid medication gave satisfactory results (dose 0.15 gm. daily).—G. V.

(THYROID) Are iodides foods? McClendon (J. F.), Science (N. Y.), 1922, n. s. **55**, 358-361.

A discussion of the distribution of iodine from sea water spray and its relation to goiter prevention. The use of an impure salt from sea water is suggested in order to furnish iodine.—F. A. H.

(THYROID) Two cases of myxedema in children. Margulis (B. I.), Prakt. Vrach (Petrogr.), 1916, **15**, 170-183.

Reference verified from Index Medicus.

Extensive bone formation in the THYROID. Meyer (H. W.), Proc. N. York Path. Soc. (N. Y.), 1919, **19**, 70.

A very brief presentation of an adnomatous thyroid "with not only deposition of lime salts within the stroma, but also extensive formation of true bone."—J. P. S.

(THYROID) Etiology of chorea (Sulla etio-patogenesi della corea del Sydenham). Milio (G.), Pediatria (Napoli), 1921, **29**, 360-363.

Silvestri is quoted to the effect that hyperthyroidism may be a cause of chorea, since it developed in two children being treated with thyroid preparation for adenoids and ceased when the thyroid was discontinued. Simonini relates the disease to parathyroid insuf-

ficiency since, in a woman who died after repeated attacks of chorea, he found hypoplasia of these glands.—G. V.

(THYROID) Endemic goiter; histology and therapy (Gozzo endemico; istologia e terapia). Muggia (G.), Riforma med. (Napoli), 1921, **37**, 738.

The author calls this kind of goiter "mountain thyroid" and he claims that where the goiter is endemic there is no such a thing as a healthy thyroid. He found, besides the well known hypertrophy, small follicles deprived of colloid with cubical epithelium, showing more or less fatty degeneration. A gradual connective hyperplasia follows and finally, cystic degeneration and calcification. The connective hyperplasia is precocious and the volume of the gland has no connection with the severity of the lesion. Muggia emphatically denies infection as a cause of goiter and refers it to geologic and meteorologic conditions (pressure, rarefaction of air and deficient oxygenation). Opotherapy proves very efficacious and has to be continued until the size of the gland approaches normal. Little improvement in the intelligence has been seen.—G. V.

(THYROID) Cases of Graves' disease. Nordentoft (S.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 31-36.

The author has treated 150 cases of Graves' disease with x-rays. No mortality resulted and they were for the most part improved or cured. He describes more in detail two severe cases, those of a mother and a daughter, who were cured. He considers the dangers from x-ray treatment very slight. He maintains the desirability of considering a thymic factor in Graves' disease, which he has mentioned in former articles.—K. H. K.

(THYROID) The toxic goitre. Ohara (H.), Nisshin Igaku, **10**, No. 10; abst., Jap. Med. World (Tokyo), 1921, **1**, 23.

Leucocytes markedly increased the blood viscosity (3.7 to 6.2, mean 5.12) possibly due to increase of leucocytes. Thyroid secretion in Basedow's disease caused an increase of **adrenalin** and sugar content of the blood. Coagulability was decreased, possibly due to antolysis of fibrin due to thyroid secretion. The resistance of the erythrocytes was markedly increased but fell to normal following extirpation of the gland. Alimentary adrenal glycosuria may be applied to determine the severity of the disease. The author concludes that extirpation of the thyroid is an ideal treatment in bringing the changed blood to normal.—R. G. B.

(THYROID) Toxic goiter. Ohara (H.), Nisshin Igaku, **11**, No. 1; abst., Jap. Med. World (Tokyo), 1922, **2**, 55.

The author dealt with the influence of toxic goiter on the circulatory organs. The heart is especially affected.—R. G. B.

(THYROID) Anemia and goiter (II Communication). Ohara (H.), Nisshin Igaku, **10**, No. 12; abst., Jap. Med. World (Tokyo), 1922, **2**, 22.

There may be anemic manifestation in simple and exophthalmic goiter but true anemia is not necessarily present and so when present is not necessarily due to the goiter.—R. G. B.

(THYROID: PARATHYROIDS) Studies on the amino-acid nitrogen content of the blood. Okada (S.) & Hayashi (T.), J. Biol. Chem. (Balt.), 1922, **51**, 121-133.

These studies of the amino-acid nitrogen content of the blood of dogs and rabbits show that the removal of the thyroid gland or of the parathyroids, from which latter procedure tetany is developed, causes an appreciable change in this fraction of the blood nitrogen. Five cases of Graves' disease were examined and the amino-acid content of the blood was normal in all. The thorough removal of the pancreas causes a transient increase of amino-acids in the blood. When a part of the pancreas is left under the skin in connection with the circulation of the blood the amino-acid nitrogen remains normal.—F. S. H.

The glycogen content of the liver and muscles in THYROIDECTOMIZED animals (Sur la teneur en glycogène du foie et des muscles chez des animaux éthyroïdés). Parhon (Marie), J. de physiol. et de path. gén. (Par.), 1921, **19**, 198-201.

Mme. Parhon reviews briefly the literature dealing with the blood sugar, glycogen content of liver and muscles, and sugar tolerance in thyroidectomized rabbits, dogs, sheep and guinea pigs. Observations are reported on the glycogen content of the liver and muscles of five normal guinea pigs, five thyroidectomized guinea pigs, two normal sheep and three thyroidectomized sheep. The guinea pigs were adults while the sheep were about six weeks old. The thyroidectomized guinea pigs were allowed to live six or seven months and the sheep fourteen to fifteen months before sacrificing. The glycogen content of the liver of the thyroidectomized animals was slightly less than that of the controls. This could not be explained on the basis of increased consumption. The author therefore believes that in thyroidectomized animals the sugar absorption from the alimentary tract is slower and less complete than normal, and that this also is the most probable explanation of the so-called increased alimentary tolerance for sugar in thyroidectomized animals. (The diet does not appear to have been controlled and the very long period the animals were allowed to live after thyroidectomy gives sufficient time for compensation which we know occurs with great frequency in animals.)—D. M.

(THYROID) Exophthalmic goiter with marked vasomotor symptoms (Forma frusta di morbo di Flaiani-Basedow con sintomi spiccati di natura vasomotoria). Pennisi (A.), Riv. osp. (Roma), 1917, **6**, 712.

Reference verified from Index Medicus.

The treatment of carcinoma of the THYROID by the Roentgen rays and radium. Pfahler (G. E.), Am. J. Roentgenol. (Detroit), 1922, **9**, 20-25.

Dr. Pfahler finds no record of the treatment of carcinoma of the thyroid by radiation, but suspects that other cases have been reported under more general terms. His experiences have extended over a period of eleven years and the results have been generally most gratifying, for in nearly all instances the treatment was used in an otherwise hopeless group and yet the results have been in some cases brilliant. He places on record ten cases. Case 1 was treated in 1910 and had been previously operated upon three times for carcinoma of the thyroid and recurrences. The treatment given in 1910 was for a recurrence consisting of an indurated mass in the region of the wound, immediately above the clavicle on the right side and another indurated moveable tumor mass, 2.5 cm. in diameter, located below the mastoid on the right side. Under treatment the patient apparently regained health for about a year and there was no local recurrence at any time, but about eighteen months after beginning treatment she developed signs of metastasis in the first cervical vertebra, from which she died two years and one month after beginning treatment. Case 2 involved a large tumor of the right lobe of the thyroid extending down into the upper mediastinum. The tumor was radiated in 1911. The patient was well when last heard from in 1918. Case 3 was treated in 1913 after operation by Dr. John B. Deaver in which he was unable to remove all of the diseased tissue. The patient was still well September 19, 1921. Case 4 had been operated upon twice, first under the diagnosis of branchial cyst involving the right side of the neck and second for a recurrence of the tumor involving the right lobe of the thyroid. This was found by microscopical examination to be adeno-sarcoma. A re-study of the original tumor showed it to be malignant. At the time of beginning x-ray treatment radioscopy of the chest showed an abnormal shadow about the roots of the right lung and extending upward along the right mediastinum. The patient was treated in 1917 and is still well. Case 5 was referred for treatment in 1917 after an operation in which all of the diseased tissue could not be removed. The disease was proven microscopically to be malignant. At the beginning of treatment there was general induration about the tissues of the neck and around the line of incision. He was treated during six months when he appeared to be perfectly well. He then discontinued treatment and passed from observation.

He died in November, 1919, with evidence of metastasis in the spine. There was no local recurrence. Case 6 was treated in 1917. Within a period of two and a half years he had been operated upon four times for carcinoma of the thyroid and recurrences. Under x-ray treatment he showed some improvement, but died of mediastinal disease about six months after he was originally referred for treatment. Case 7 was referred for treatment in 1919 after exploratory operation in which a section was removed and the tumor found to be inoperable. Microscopical examination showed this to be carcinoma. Under x-ray and radium treatment he has finally recovered and is still well. Case 8 was operated upon by Dr. John B. Deaver for carcinoma of the thyroid and referred for post-operative treatment three weeks after operation. She was referred June 14, 1919, and was reported well September 9, 1921. Case 9 was referred by Dr. H. M. Foss, who had operated upon the patient for carcinoma of the thyroid. The tumor was found to be inoperable and tissue taken for microscopical examination proved to be carcinoma. Treatment began September 10, 1919; the patient was still well September, 1921. Case 10, a female, age 68, was referred for treatment on account of an indurated, adherent tumor of the thyroid, which had all clinical appearances of carcinoma. She was first treated May 12, 1921, and was still well at the time of this report.

The following conclusions can be drawn: Every case of carcinoma of the thyroid that has been operated upon should receive as soon as possible at least two thorough courses of Roentgen-ray treatment and more if traces of the disease remain. If the diagnosis of carcinoma of the thyroid can be made without operation, a reasonably good hope of success from radiation treatment can be entertained. Recurrent cases can be made to respond to treatment and the recurrence can be made to disappear, but definite metastases are not likely to be controlled. Radium can be combined with the Roentgen-ray treatment to good advantage in carcinoma of the thyroid when the tumor has become definitely localized or when it ceases to respond to the Roentgen-rays.—Author's Abst.

(THYROID) Carcinomatous transformation of a lingual goiter. Ray (H. M.), Proc. N. York Path. Soc. (N. Y.), 1918, **18**, 12-14.

A brief report of a case of lingual goiter, which measured 5 cm. in diameter. The tumor showed "definite evidence of carcinomatous transformation."—J. P. S.

(THYROID) Iodine and the metamorphosis of Ammocoetes branchialis into Petromyzon planeri Bloch (L'iode et la métamorphose de l'Ammocoetes branchiales en Petromyzon planeri Bloch). Rémy (P.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 129-131.

Experiments were made on ammocoetes. The larvae were kept in water containing iodothyrin, or were given injections of iodothy-

rin, thyroid extract, emulsion of iodoform, etc. Apparently there were no cases of accelerated metamorphosis,—no silver color appearing in the ventral integument, or no appearance of eyes, which are the first stages in metamorphosis. Iodine, the accelerator of metamorphosis in batrachians, seems not to act as such on cyclostomes. Metamorphosis is regulated by a substance different from that of batrachians.—T. C. B.

The modifications induced by THYROID treatment on the somatic structure in congenital sporadic infantile myxedema (Le modificazioni prodotte dalla cura tiroidea sulla struttura somatica nel mixedema congenito sporadico infantile). Rosso (M.), Riv. di clin. pediat. (Firenze), 1921, —, —, fasc. 7; abst. Terapia (Milan.), 1921, **11**, 17.

After careful observations the author came to the conclusion that the thyroid treatment in congenital sporadic infantile myxedema altered the megalosplanchnic growth of the patient into normal. The growth was in length; there was hardly any change in the transverse diameters. This result accords with what is thought nowadays about the morphogenetic influence of the thyroid secretion.

—G. V.

(THYROID) Goiter in relation to the trachea, especially from a tracheoscopic point of view. Schmiegelow (E.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 26-31.

The author mentions two cases in which a retrosternal goiter compressed the trachea. Tracheoscopy is helpful in the diagnosis of this condition, but in many cases radioscopy alone suffices.

—K. H. K.

Diabetes with THYROID hypertrophy (Sopra un caso di diabete con ipertrofia tiroidea). Schupfer (F.), Riv. crit. di clin. med. (Firenze), 1917, **17**, 573; 586; 601; Pensiero med. (Milano), 1916, **6**, 547; 570.

Reference verified from Index Medicus.

Integumentary changes in the sheep following THYROIDECTOMY and administration of THYROXIN. Simpson (S.), Am. J. Physiol. (Balt.), 1922, **59**, 445-446.

Photographs of two rams were shown. Both were born May 7, 1920. From one the thyroid was removed at the age of five months; the other was kept as control. The horns were the same size in both at the time of operation. In November, 1921, in the thyroidectomized animal the left horn measured six inches; the right four inches. In the normal control the horns measured twenty-one inches. In a thyroidectomized lamb—a cretin dwarf—aged nine months, thyroxin was given subcutaneously in half milligram doses

daily. After a fortnight of treatment, although in the middle of winter in Western New York, the wool began to fall out, leaving the skin denuded. When the amount of thyroxin was reduced a normal fleece developed. Probably the original dose was excessive.
—T. C. B.

Blood flow and oxygen metabolism of the THYROID gland. Knowlton (F. P.), Dooley (M. S.) & Curtiss (A. N.), Am. J. Physiol. (Balt.), 1922, **59**, 446-447.

The measurement of the blood flow and gaseous metabolism of the thyroid was undertaken with the hope that the method might be used to study the activities of the gland. The method of Barcroft and Brodie was used. The resting condition in dogs was studied. The average result for the blood flow was 3.55 cc. per gram per minute; for the oxygen consumption, 0.0927 cc. per gram per minute.
—T. C. B.

(THYROID) The use of iodized table salt in the prevention of goiter. Sloan (H. G.), Ohio M. J. (Columbus), 1921, **17**, 172-174.

After reviewing the general aspect of goiter prevention and the relation of iodine thereto, Sloan discusses methods of iodinization of the body. Iodine may be taken into the body by inhalation, by absorption from the gastro-intestinal tract or by absorption through the skin. The need of iodine may generally be met by painting the skin with iodine, through the use of Syrup of Iron Iodide, one drop per year of age, daily during alternate months, or through sodium iodide in 0.2 gm. doses, daily, for ten consecutive school days in the spring and autumn. In the Swiss schools it has become a custom to suspend wide-mouthed bottles of iodine in the school room in order that the children may inhale the fumes. Sloan points out that each of these is a troublesome method likely to be neglected until signs of thyroid enlargement actually appear. To obviate this neglect, he recommends the introduction into all table salt of a small percentage of sodium iodide; one portion of sodium iodide to five thousand of salt is said to be sufficient to maintain a saturation of the normal thyroid gland which contains about 30 milligrams of iodine. This practice, the writer believes, will eliminate goiter in the second generation. At the same time it is not likely to affect badly either exophthalmic or mildly toxic goiters.—C. P. McC.

(THYROID) The surgical treatment of Graves' disease. Soelling (H. A.), Hosp.-Tid. (Copenhagen), 1921, **64**, Danish med. Soc. reports, 7-20.

The author compares the results from about 100 cases of Graves' disease surgically treated, with other cases in literature. In the acute cases (22) the results ordinarily were bad in both medical and surgical treatment. In 90 chronic cases better results were

obtained from the surgical treatment than in 80 cases which were not operated upon. He has the impression that thymectomy is not advisable.—K. H. K.

Fibromyoma of the uterus accompanied by HYPERTHYROIDISM. Thompson (W. H.), Am. J. Obst. & Gyn. (St. Louis), 1921, **2**, 621-628.

After reviewing the relations of the thyroid to menstruation and pregnancy, the author reports three cases suggesting to him that the hyperplasia and cell proliferation of the uterus found in fibromyomas may activate the thyroid, and that the myocardial weakness so often found with fibromyomas may be due to hyperthyroidism and not directly to the tumor.—E. N.

The relation between food and THYROID. Tsuji (K.), Nihon Naikagakkwai Zasshi, **9**, No. 5; Abst., Jap. Med. World (Tokyo), 1922, **2**, 45.

The author previously dealt with a substance in raw cow's milk which acted as a hormone on the thyroid. Egg yolk and butter caused an increase in the weight of the thyroid, and an increased function and histological glandular structure. Feeding with a mixture of pure albumin, carbohydrate, fat and salts caused atrophy of the thyroid with corresponding relative effects on other organs. He concludes that egg yolk and raw milk contain substances which stimulate the thyroid.—R. G. B.

Functions of the THYROID with special reference to the relation to diet. Tsuki (K.), Igaku Chuwo Zasshi (Tokyo), No. 352; Abst., Jap. Med. World (Tokyo), 1921, **1**, 25.

The author fed to animals food deficient in vitamine and observed their development and state of nutrition during the winter. Deterioration of, as extirpation of, the thyroid resulted in stunted growth or emaciation and a remarkable change in the alimentary and **genital glands.** Vitamine deficiency caused stunted growth or emaciation with deranged thyroid function, though it was still in an active state. The glandular organs underwent changes similar to those following thyroid extirpation. The author concludes that vitamines in the food has a hormone-like action upon the thyroid.
—R. G. B.

(THYROID) A series of fifty cases of exophthalmic goiter treated by operation. Walron (A. J.), Practitioner (Lond.), 1917, **99**, 309-338.

The importance of selecting a suitable time for operation to avoid exacerbations of the disease is emphasized. The technique of the operation is described in detail, special stress being given to control of bleeding. Post-operative treatment is then outlined, with

attention directed to the diet (following Ochsner's scheme). The author's mortality was 4 per cent. Some of the patients have been followed for four years. Of the 50 patients, 25 were completely cured; 17 were greatly relieved, able to return to work and normal living, but still showing signs of the disease; 4 were slightly relieved; 2 were not heard from after leaving the hospital; 2 died. Brief records of the fifty cases supplement the article. The author declares the surgical mortality much lower than that resulting from medical and x-ray treatment, which he places at 25 per cent. Many of his patients had received non-surgical treatment for long periods of time prior to consulting him. He is fair enough to recognize, however, that those patients who are cured or greatly improved by medical measures are not apt to come under the observation of the surgeon.—H. L.

(THYROID) Further notes on the control of goiter in the new born. Welch (H.), J. Am. Vet. Assn. (Ithaca), 1918, **53**, 523-526.

A report of experiences with congenital goiter in pigs, lambs, etc., in Montana and the remarkable beneficial effects of the administration of potassium iodide to mothers during pregnancy in its prevention. It is recommended that two grains of potassium iodide be administered daily per animal, using sugar of milk as a vehicle, to be continued for 90 to 100 days. This makes the cost of treatment about 50c per head. He thinks the cost might be reduced, though the present figure seems low enough when compared with the results obtained.—D. M.

(THYROID) Discussion on the medical and surgical treatment of Graves' disease. Williams (L.), Proc. Roy. Soc. Med. (Lond.), 1921, **14** (Clin. Sect.), 54.

Writers are still far from unanimous as to which gland or glands of internal secretion are responsible for Graves' disease. In a discussion on the medical and surgical treatment of Graves' disease at the Royal Society of Medicine, Williams contended that Graves' disease is not only not a hyperthyroidism but is not a disease of the thyroid gland at all. He stated that the most outstanding feature of the complaint, namely, exophthalmos and cardiac troubles, are due to the implication of other glands, the exophthalmos being due to **adrenal** excess and the cardiac symptoms to enlargement of the **thymus.** He considered that this enlargement, which occurred in 85 per cent of the cases, caused not only cardiac symptoms by pressure on the base of the heart and great vessels, but also many of the nervous symptoms by pressure on the vagus, sympathetic, and phrenic, as well as mental symptoms by interfering with drainage from the brain. He regarded Graves' disease as due to toxemia in which all the members of the endocrine hierarchy are involved. The only way of treating the disease, in

his opinion, is by discovering the source of the toxin and eliminating it. In a large percentage of cases the toxin is gastro-intestinal, and can be successfully dealt with only by dieting and, if necessary, intestinal antiseptics.—Med. Sci., 5, 300.

Illustrative cases of malignant tumors of the THYROID. Wilson (L. B.), Surg. Clin. N. Am. (Phila.), 1921, 1, 1291-1306.

Wilson believes that malignancy of the thyroid is of relatively frequent occurrence, that many cases start as adenomas in the third decade and progress slowly to malignancy. This long persistence, together with the resemblance of the tumor to other thyroid enlargements, is largely responsible for errors in diagnosis. Of 290 patients with malignant tumors of the thyroid seen in the Mayo Clinic during twenty years, 158 developed goiter before the age of thirty; 61 noticed thyroid enlargement less than a year before diagnosis; one-fourth had accelerated thyroid growth during the year preceding diagnosis; one-third had continuous growth for ten years. The author suggests careful histological examination of all nodular tumors, considering all markedly proliferating adenomas potentially malignant.—C. R.

(THYROID) Graves' disease and manic-depressive insanity. Wimmer (A.), Bibliot. f. Læger (Copenhagen), 1919, 3, 262-278.

We cannot necessarily conclude that there is an etiologic connection between Graves' disease and insanity in the cases where they are combined. The literature presents a great difference of opinion on this point. Many authors who have suggested "Basedowian insanity" have not considered sufficiently other etiologic factors (alcoholism, syphilis, etc.). The connection is most probable in cases of delirium or confusion which may point to a toxic condition, but only a minority of the published cases of "Basedowian insanity" are of this kind. The most common insanity in Graves' disease is the manic-depressive type. Statistics, however, show that this combination must be regarded as only occasional. The author describes in detail 4 cases which point to the lack of constancy of the combination; especially, there is no connection between the time of incidence of Graves' disease and insanity.—K. H. K.

Phosphorus and ash content of the human THYROID (Sur la teneur en phosphore et en cendres du corps thyroide du l'homme). Zunz (E.), Réunion soc. belge biol., 1920, 146-147.

Analyses were made of 32 thyroid glands of average weight obtained from normal men killed in the war. The dry residue contained from 0.89% to 1.82%, av. 1.38% P., and from 2.60% to 5.11%, av. 3.86% ash. The ratio P:N ranged from 0.062 to 0.140, av. 0.094. The ratio I:N ranged from 0.004 to 0.029, av. 0.0154. The ratio I:P ranged from 0.025 to 0.422, av. 0.1813.—Chem. Abst.

(THYROID, HYPOPHYSIS) A case of idiocy. de Vries (E.), Maandbl. v. Specialistische Geneesk. (Amst.), 1922, **5**, 8.

An idiotic girl of 19, of infantile type, has mammae somewhat developed and a pelvis of female form. This is probably due to an endocrine disturbance, especially hypothyroidism and hypopituitarism.—J. K.

Physiology of the TONSILS (Sulla fisiologia delle amigdale). Farmachidis (C. B.), Riforma med. (Napoli), 1921, **37**, 923-924.

After numerous clinical observations and a great deal of experimental research on the tonsils in regard to glycosuria, since 1914, the author comes to the following conclusions. Acute pharyngo-tonsillitis may determine a transitory glycosuria. Glycosuria can be evoked in animals by experimental irritation of the tonsils. Ox tonsil extract shows glycolytic action even in vitro. The glycolytic action is more manifest if the extract acts on glycose in urine rather than in distilled water. Its action is demonstrable in glycosuric animals, even after removal of the pancreas. Ox tonsil extract is antagonistic to the action of adrenalin. The action is more evident if the extract is given intravenously. Finally, Farmachidis claims that an efficacious action is obtained through tonsil extract in glycosuria as well as in the diabetic syndrome. From these observations he infers that the tonsils are "among the organs apt to determine glycosuria through their alteration" and he thinks they are endocrine organs. He quotes the experiment of Fleischmann (1921). The discussion is occasioned by the theory of infection through the tonsils, as published by Blodgett in Penn. M. J., 1921.—G. V.

The UTERUS as an endocrine organ (L'utero sede di secrezione interna). Fornero & Balli, Radiol. med. (Torino), 1921; Abst., Riforma med. (Napoli), 1921, **37**, 707.

The authors claim that the uterus has a great endocrine value; they object to too hasty removal of the organ, on account of the consequent endocrine imbalance. By x-ray treatment of the uterus they seem to have obtained renewal of uterine hormone production and correction of utero-ovarian insufficiency.—G. V.